

Substituted pyridine compounds and methods of use

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Selected novel substituted pyridine compounds are effective for prophylaxis and treatment of diseases, such as TNF- alpha , IL-1 beta , IL-6 and/or IL-8 mediated diseases, and other maladies, such as pain and diabetes. The invention encompasses novel compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions and methods for prophylaxis and treatment of diseases and other maladies or conditions involving inflammation, pain, diabetes, cancer and the like. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

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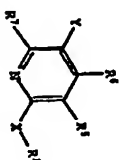
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SUBSTITUTED PYRIDINE COMPOUNDS AS ANTI-INFLAMMATORY AGENTS

BACKGROUND OF THE INVENTION

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The present invention comprises a new class of compounds useful in treating diseases, such as TNF- α , IL-1 β , IL-6 and/or IL-8 mediated diseases and other maladies, such as pain, cancer, and diabetes. In particular, the compounds of the invention are useful for the prophylaxis and treatment of diseases or conditions involving inflammation. This invention also relates to intermediates and processes useful in the preparation of such compounds.

15 Interleukin-1 (IL-1) and Tumor Necrosis Factor α (TNF- α) are pro-inflammatory cytokines secreted by a variety of cells, including monocytes and macrophages, in response to many inflammatory stimuli (e.g., lipopolysaccharide - LPS) or external cellular stress (e.g., osmotic shock and peroxide).

Elevated levels of TNF- α and/or IL-1 over basal levels have been implicated in mediating or exacerbating a number of disease states including rheumatoid arthritis; Pagets disease; osteoporosis; multiple myeloma; uveitis; acute and chronic myelogenous leukemia; pancreatic β cell destruction; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; muscle degeneration; cachexia; Reiter's syndrome; type I and type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever, and myalgias due to infection.

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HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses (including HSV-1, HSV-2), and herpes zoster are also exacerbated by TNF- α .

It has been reported that TNF- α plays a role in head trauma, stroke, and ischemia. For instance, in animal models of head trauma (rat), TNF- α levels increased in the contused hemisphere (Shohami et al., *J. Cereb. Blood Flow Metab.* **14**, 615 (1994)). In a rat model of ischemia wherein the middle cerebral artery was occluded, the levels of TNF- α mRNA of TNF- α increased (Feurstein et al., *Neurosci. Lett.* **164**, 125 (1993)). Administration of TNF- α into the rat cortex has been reported to result in significant neutrophil accumulation in capillaries and adherence in small blood vessels. TNF- α promotes the infiltration of other cytokines (IL-1 β , IL-6) and also chemokines, which promote neutrophil infiltration into the infarct area (Feurstein, *Stroke* **25**, 1481 (1994)). TNF- α has also been implicated to play a role in type II diabetes (Endocrinol. **130**, 43-52, 1994; and Endocrinol. **136**, 1474-1481, 1995).

TNF- α appears to play a role in promoting certain viral life cycles and disease states associated with them. For instance, TNF- α secreted by monocytes induced elevated levels of HIV expression in a chronically infected T cell clone (Clouse et al., *J. Immunol.* **142**, 431 (1989)). Lahdevirta et al., (*Am. J. Med.* **85**, 289 (1988)) discussed the role of TNF- α in the HIV associated states of cachexia and muscle degradation.

20 TNF- α is upstream in the cytokine cascade of inflammation. As a result, elevated levels of TNF- α may lead to elevated levels of other inflammatory and proinflammatory cytokines, such as IL-1, IL-6, and IL-8.

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Elevated levels of IL-1 over basal levels have been implicated in mediating or exacerbating a number of disease states including rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; ulcerative colitis; anaphylaxis; muscle degeneration; cachexia; Reiter's syndrome; type I and type II diabetes; bone resorption diseases; ischemia reperfusion injury; atherosclerosis; brain trauma; multiple sclerosis; sepsis; septic shock; and toxic shock syndrome. Viruses sensitive to TNF- α inhibition, e.g., HIV-1, HIV-2, HIV-3, are also affected by IL-1.

TNF- α and IL-1 appear to play a role in pancreatic β cell destruction and diabetes. Pancreatic β cells produce insulin which helps mediate blood glucose homeostasis. Deterioration of pancreatic β cells often accompanies type I diabetes. Pancreatic β cell functional abnormalities may occur in patients with type II diabetes. Type II diabetes is characterized by a functional resistance to insulin. Further, type II diabetes is also often accompanied by elevated levels of plasma glucagon and increased rates of hepatic glucose production. Glucagon is a regulatory hormone that attenuates liver gluconeogenesis inhibition by insulin. Glucagon receptors have been found in the liver, kidney and adipose tissue. Thus glucagon antagonists are useful for attenuating plasma glucose levels (WO 97/16442, incorporated herein by reference in its entirety). By antagonizing the glucagon receptors, it is thought that insulin responsiveness in the liver will improve, thereby decreasing gluconeogenesis and lowering the rate of hepatic glucose production.

In rheumatoid arthritis models in animals, multiple intra-articular injections of IL-1 have led to an acute and destructive form of arthritis (Chandrasekhar et al., *Clinical Immunol Immunopathol.* 55, 382 (1990)). In

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studies using cultured rheumatoid synovial cells, IL-1 is a more potent inducer of stromelysin than is TNF- α (Firestein, *Am. J. Pathol.* 140, 1309 (1992)). At sites of local infection, neutrophil, lymphocyte, and monocyte emigration has been observed. The emigration is attributed to the induction of chemokines (e.g., IL-8), and the up-regulation of adhesion molecules (Dinarello, *Eur. Cytokine Netw.* 5, 517-531 (1994)).

IL-1 also appears to play a role in promoting certain viral life cycles. For example, cytokine-induced increase of HIV expression in a chronically infected macrophage line has been associated with a concomitant and selective increase in IL-1 production (Folks et al., *J. Immunol.* 136, 40 (1986)). Beutler et al. (*J. Immunol.* 135, 3969 (1985)) discussed the role of IL-1 in cachexia. Baracos et al. (*New Eng. J. Med.* 308, 553 (1983)) discussed the role of IL-1 in muscle degeneration.

In rheumatoid arthritis, both IL-1 and TNF- α induce synoviocytes and chondrocytes to produce collagenase and neutral proteases, which leads to tissue destruction within the arthritic joints. In a model of arthritis (collagen-induced arthritis (CIA) in rats and mice), intra-articular administration of TNF- α either prior to or after the induction of CIA led to an accelerated onset of arthritis and a more severe course of the disease (Brahn et al., *Lymphokine Cytokine Res.* 11, 253 (1992); and Cooper, *Clin. Exp. Immunol.* 898, 244 (1992)).

IL-8 has been implicated in exacerbating and/or causing many disease states in which massive neutrophil infiltration into sites of inflammation or injury (e.g., ischemia) is mediated by the chemotactic nature of IL-8, including, but not limited to, the following: asthma, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, cardiac and renal reperfusion injury,

thrombosis and glomerulonephritis. In addition to the chemotaxis effect on neutrophils, IL-8 also has the ability to activate neutrophils. Thus, reduction in IL-8 levels may lead to diminished neutrophil infiltration.

5 Several approaches have been taken to block the effect of TNF- α . One approach involves using soluble receptors for TNF- α (e.g., TNFR-55 or TNFR-75), which have demonstrated efficacy in animal models of TNF- α -mediated disease states. A second approach to

10 neutralizing TNF- α using a monoclonal antibody specific to TNF- α , c α 2, has demonstrated improvement in swollen joint count in a Phase II human trial of rheumatoid arthritis (Feldmann et al., *Immunological Reviews*, pp. 195-223 (1995)). These approaches block the effects of

15 TNF- α and IL-1 by either protein sequestration or receptor antagonism.

The present invention also relates to a method of treating cancer which is mediated by Raf and Raf-inducible proteins. Raf proteins are kinases activated

20 in response to extracellular mitogenic stimuli such as PDGF, EGF, acidic FGF, thrombin, insulin or endothelin, and also in response to oncoproteins such as v-src, v-sis, and v-fms. Raf functions downstream of ras in signal transduction from the cellular membrane to the nucleus. Compounds in the present invention may be

25 oncolytics through the antagonism of Raf kinase.

Antisense constructs which reduce cellular levels of c-Raf and hence Raf activity inhibit the growth of rodent fibroblasts in soft agar, while exhibiting little or no general cytotoxicity. This inhibition of growth in soft

30 agar is highly predictive of tumor responsiveness in whole animals. Moreover Raf antisense constructs have shown efficacy in reducing tumor burden in animals. Examples of cancers where Raf kinase is implicated by overexpression include cancers of the brain, larynx, lung, lymphatic system, urinary tract and stomach,

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including hystocytic lymphoma, lung adenocarcinoma and small cell lung cancers. Other examples include cancers involving overexpression of upstream activators of Raf or Raf-activating oncogenes, including pancreatic and

5 breast carcinoma.

Substituted imidazole and pyrrole compounds have been described for use in the treatment of cytokine mediated diseases by inhibition of proinflammatory cytokines, such as IL-1, IL-6, IL-8 and TNF.

10 Substituted imidazoles for use in the treatment of cytokine mediated diseases have been described in US Pat. 5,593,992; WO 93/14081; WO 97/18626; WO 96/21452; WO 96/21654; WO 96/40143; WO 97/05878; WO 97/05878; (each of which is incorporated herein by reference in its entirety). Substituted imidazoles for use in the

15 treatment of inflammation has been described in US Pat. 3,929,807 (which is incorporated herein by reference in its entirety). Substituted pyrrole compounds for use in the treatment of cytokine mediated diseases have been

20 described in WO 97/05877; WO 97/05878; WO 97/16426; WO 97/16441; and WO 97/16442 (each of which is incorporated herein by reference in its entirety).

Substituted 2-aminopyridine compounds have been described as nitric oxide synthase inhibitors for use in

25 the treatment of inflammation, neurodegenerative disorders and disorders of gastrointestinal motility in WO 96/18616 and WO 96/18617.

Diaryl substituted pyridine compounds have been described for use in the treatment of inflammation and

30 inflammation related disorders in WO 96/24584 and US 5,596,008.

US 3,980,652, US 3,991,057 and US 4,002,629

describe piperazinyl substituted pyridine compounds for use as anti-inflammatory and cardiovascular agents.

35 JP 6135934 describes substituted pyridine compounds as phospholipase A2 inhibitors for use as antiproliferative and anti-pancreatitis agents. GB 1,189,188 describes

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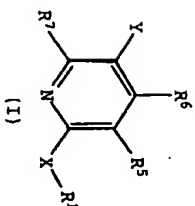
pyrimidin-2-ylamino substituted pyridine compounds as therapeutically valuable compounds for use as anti-phlogistic agents.

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BRIEF DESCRIPTION OF THE INVENTION

The present invention comprises a new class of compounds useful in the prophylaxis and treatment of diseases, such as TNF- α , IL-1 β , IL-6 and/or IL-8 mediated diseases and other maladies, such as pain, cancer, and diabetes. In particular, the compounds of the invention are useful for the prophylaxis and treatment of diseases or conditions involving inflammation. Accordingly, the invention also comprises pharmaceutical compositions comprising the compounds, methods for the prophylaxis and treatment of TNF- α , IL-1 β , IL-6 and/or IL-8 mediated diseases, such as inflammatory, pain and diabetes diseases, using the compounds and compositions of the invention, and intermediates and processes useful for the preparation of the compounds of the invention.

The compounds of the invention are represented by the following general structure:



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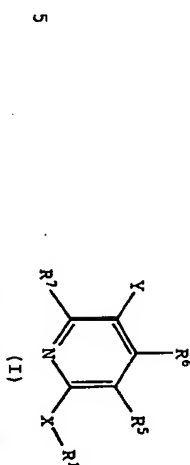
wherein R¹, R⁵, R⁶, R⁷, X and Y are defined below.

The foregoing merely summarizes certain aspects of the invention and is not intended, nor should it be construed, as limiting the invention in any way. All patents and other publications recited herein are hereby incorporated by reference in their entirety.

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DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided compounds of the formula:



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or a pharmaceutically acceptable salt thereof, wherein

X is O, S, S(O), S(O)₂, or NR²; preferably, X is O, S or NR²; more preferably, X is O or NR²; most preferably, X is NR²;

Y is -C(O)-NR³-R⁴ or -NR⁴-C(O)-R³;

R¹ is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of alkyl, halo, haloalkyl, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸- or R¹⁸-Z¹⁸-alkyl;

preferably, R¹ is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of C₁-C₆ alkyl, halo, C₁-C₆ haloalkyl of 1-3 halo radicals, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸- or R¹⁸-Z¹⁸-C₁-C₆ alkyl;

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more preferably, R¹ is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl of 1-3

halo radicals, cyano, azido, nitro, amidino, $R^{18}-Z^{18}$ - or $R^{18}-Z^{18}-C_1-C_4$ alkyl;

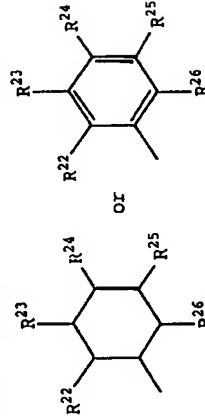
provided that the total number of aryl, heteroaryl,

5 cycloalkyl and heterocyclyl radicals in R^1 is 1-3,

preferably, 1-2, and provided when Y is $-NR^4-C(O)-R^3$ and

X is O or S, R^1 is other than a 2-pyrimidinyl radical;

more preferably, R^1 is a radical of the formula



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wherein R^22 , R^23 , R^24 , R^25 and R^26 are each independently a radical of hydrogen, C_1-C_4 alkyl, halo, trifluoromethyl, cyano, azido, nitro, amidino, $R^{18}-Z^{18}$ - or $R^{18}-Z^{18}-C_1-C_4$

alkyl; provided at least one of R^21 , R^22 , R^23 , R^24 and R^25 is hydrogen; and provided that the combined total number of aryl and heteroaryl radicals in R^2 , R^3 , R^4 , R^5 and R^6 is 0-1;

R^2 is a hydrogen or alkyl radical; preferably, R^2 is a

20 hydrogen or C_1-C_4 alkyl radical; more preferably, R^2 is a hydrogen or C_1-C_2 alkyl radical; more preferably, R^2 is a hydrogen or methyl radical; and most preferably, R^2 is a hydrogen radical;

25 R^3 is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of alkyl, halo, haloalkyl,

cyano, azido, nitro, amidino, $R^{19}-Z^{19}$ - or $R^{19}-Z^{19}$ -alkyl;

preferably, R^3 is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl of 1-3 halo radicals, cyano,

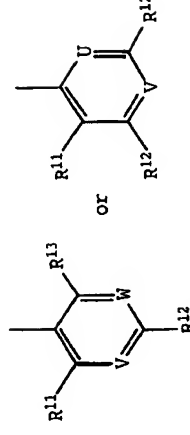
5 azido, nitro, amidino, $R^{19}-Z^{19}$ - or $R^{19}-Z^{19}-C_1-C_6$ alkyl;

more preferably, R^3 is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of C_1-C_6 alkyl, halo, C_1-C_4 haloalkyl of 1-3 halo radicals,

10 cyano, azido, nitro, amidino, $R^{19}-Z^{19}$ - or $R^{19}-Z^{19}-C_1-C_4$ alkyl;

provided that the total number of aryl and heteroaryl radicals in R^3 is 1-3, preferably, 1-2; and provided when Y is $-C(O)-NR^{34}$, R^3 is other than a phenyl or naphthyl having an amino, nitro, cyano, carboxy or alkoxy-carbonyl substituent bonded to the ring carbon atom adjacent to the ring carbon atom bonded to $-NR^4$;

more preferably, R^3 is a radical of the formula



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wherein

U is $C-R^{13}$ or N;

25 V and W are each independently $C-R^{12}$ or N;

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R^{11} and R^{13} are each independently a radical of hydrogen, C_1-C_4 alkyl, halo, trifluoromethyl, cyano, azido, nitro, amidino or $R^{19}-Z^{19}$; preferably, R^{11} and R^{13} are each independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, cyano, azido, nitro, amidino, $R^{18}-O-$, $R^{19}-S(O)_2-$, $R^{19}-O-C(O)-$, $R^{19}-C(O)-$, or $R^{19}-NR^{21}-S(O)_2-$;

each R^{12} is independently a radical of hydrogen, C_1-C_6 alkyl, halo, C_1-C_4 haloalkyl of 1-3 halo radicals, $R^{31}-Z^{31}$ or $R^{31}-Z^{31}-C_1-C_4$ alkyl; preferably, each R^{12} is independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, trifluoromethoxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, (methylamino)methyl or (dimethylamino)methyl;

provided that the combined total number of aryl and heteroaryl radicals in R^{11} , R^{12} and R^{13} is 0-1;

wherein each R^{11} is independently a hydrogen, C_1-C_4 alkyl, trifluoromethyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl or heteroaryl- C_1-C_4 alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy;

each Z^{11} is independently -O-, $-NR^{21}$ -, $-NR^{21}-C(O)-$, $-C(O)-NR^{21}$ -, $-NR^{21}-S(O)_2-$ or $-S(O)_2-NR^{21}$;

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R^4 is a hydrogen, alkyl, alkenyl, haloalkyl, haloalkenyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl or $R^{20}-Z^{20}$ -alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxy-carbonylamino, alkoxy-carbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, R^4 is a radical of hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl of 1-3 halo radicals, C_2-C_6 haloalkenyl of 1-3 halo radicals, aryl, heteroaryl, aryl- C_1-C_4 alkyl, heteroaryl- C_1-C_4 alkyl or $R^{20}-Z^{20}-C_1-C_6$ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di- C_1-C_4 alkylamino, C_1-C_5 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, (C_1-C_4 alkoxy)carbonylamino, (C_1-C_4 alkoxy)carbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, R^4 is a radical of hydrogen, C_1-C_6 alkyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl, heteroaryl- C_1-C_4 alkyl or $R^{20}-Z^{20}-C_2-C_4$ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di- C_1-C_4 alkylamino, acetylamino, halo, C_1-C_4 alkyl, alkylamino, trifluoromethyl or trifluoromethoxy;

more preferably, R^4 is a radical of hydrogen, C_1-C_6 alkyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl, heteroaryl- C_1-C_4 alkyl or $R^{20-20}-C_2-C_4$ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, methylthiol, ethylthiol, amino, methylamino, dimethylamino, ethylamino, diethylamino, acetylamino, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy;

10

more preferably, R^4 is a radical of hydrogen, methyl or ethyl radical;

wherein each R^4 is independently a hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxy-carbonylamino, alkoxy-carbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, each R^4 is independently a hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl- C_1-C_4 alkyl or heteroaryl- C_1-C_4 alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, (C_1-C_4 alkoxy)carbonylamino, (C_1-C_4 alkoxy)carbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-

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35 3 halo radicals;

more preferably, each R^6 is independently a hydrogen, C_1-C_4 alkyl, trifluoromethyl, aryl, heteroaryl, aryl- C_1-C_2 alkyl or heteroaryl- C_1-C_2 alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, acetylamino, cyano, halo, azido, C_1-C_4 alkyl, trifluoromethyl or trifluoromethoxy;

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each Z^{18} is independently -O-, -S-, -S(O)-, -S(O)-, -CO₂-, -C(O)-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)- or -S(O)-NR²¹-; preferably, each Z^{18} is independently -O-, -S-, -S(O)-, -CO₂-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)- or -S(O)-NR²¹-;

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wherein each R^{19} is independently a hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxy-carbonylamino, alkoxy-carbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

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preferably, each R^{19} is independently a hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals, aryl,

heteroaryl, aryl- C_1-C_4 alkyl or heteroaryl- C_1-C_4 alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4

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alkylsulfonyl, (C₁-C₄ alkoxy)carbonylamino, (C₁-C₄ alkoxy)carbonyl, cyano, halo, azido, C₁-C₄ alkyl, C₁-C₄ haloalkyl of 1-3 halo radicals or C₁-C₄ haloalkoxy of 1-3 halo radicals;

5 more preferably, each R¹⁹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, acetylamino, cyano, halo, C₁-C₄ alkyl, trifluoromethyl or trifluoromethoxy;

15 more preferably, each R¹⁹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy;

20 more preferably, each R¹⁹ is independently a hydrogen, methyl, ethyl, trifluoromethyl, phenyl, heteroaryl, phenylmethyl or heteroaryl-methyl radical, wherein the phenyl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, fluoro, chloro, methyl, ethyl, trifluoromethyl or trifluoromethoxy;

30 each Z¹⁹ is independently -O-, -S-, -S(O)-, -S(O)₂-, -CO₂-, -C(O)-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂- or -S(O)₂-NR²¹-; preferably, each Z¹⁹ is

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independently -O-, -S(O)₂-, -CO₂-, -C(O)-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂- or -S(O)₂-NR²¹-; more preferably, each Z¹⁹ is independently -O-, -S(O)₂-, -O-C(O)-, -C(O)-, -NR²¹-C(O)- or -NR²¹-S(O)₂-;

5 wherein each R²⁰ is independently a hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

15 preferably, each R²⁰ is independently a hydrogen, C₁-C₄ alkyl, C₁-C₄ haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₃ alkanoylamino, C₁-C₄ alkylsulfonylamino, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, (C₁-C₄ alkoxy)carbonylamino, (C₁-C₄ alkoxy)carbonyl, cyano, halo, azido, C₁-C₄ alkyl, C₁-C₄ haloalkyl of 1-3 halo radicals or C₁-C₄ haloalkoxy of 1-3 halo radicals;

30 more preferably, each R²⁰ is independently a hydrogen, C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino,

acetylamino, halo, C₁-C₄ alkyl, trifluoromethyl or trifluoromethoxy;

- 5 more preferably, each R²⁰ is independently a hydrogen, C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, methylthiol, ethylthiol, amino, methylamino, dimethylamino, ethylamino, diethylamino, acetylamino, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy;

- 10 each Z²⁰ is independently -O-, -S-, -S(O)-, -S(O)₂-, -CO₂-, -C(O)-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)- or -S(O)₂-NR²¹-; preferably, each Z²⁰ is independently -O- or -NR²¹-;

- wherein each R²¹ is independently a hydrogen or alkyl radical; preferably, each R²¹ is independently a hydrogen or C₁-C₄ alkyl radical; more preferably, each R²¹ is independently a hydrogen or methyl radical;

- R⁵ and R⁶ are each independently a hydrogen, alkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, hydroxy, hydroxyalkyl, thiol, alkylthiol, alkylsulfinyl, alkylsulfonyl, alkoxy, alkoxyalkyl, cyano, azido, nitro, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl radical;

preferably, R⁵ and R⁶ are each independently a hydrogen, C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl of 1-3 halo radicals,

C₁-C₄ haloalkoxy of 1-3 halo radicals, C₁-C₄ aminoalkyl, (C₁-C₄ alkyl)amino-C₁-C₄ alkyl, di(C₁-C₄ alkyl)amino-C₁-C₄ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₅ alkanoylamino, C₁-C₄ alkylsulfonylamino,

- 5 aminosulfonyl, C₁-C₄ alkylaminosulfonyl, di(C₁-C₄ alkyl)aminosulfonyl, hydroxy, C₁-C₄ hydroxyalkyl, thiol, C₁-C₄ alkylthiol, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, C₁-C₄ alkoxy, (C₁-C₄ alkoxy)C₁-C₄ alkyl, cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical;

more preferably, R⁵ and R⁶ are each independently a hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl,

- 15 trifluoromethoxy, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₅ alkanoylamino, hydroxy, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical;

- more preferably, R⁵ and R⁶ are each independently a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, amino, C₁-C₂ alkylamino, di(C₁-C₂ alkyl)amino, hydroxy, methoxy or ethoxy radical; most preferably, R⁵ and R⁶ are each a hydrogen radical;

- R⁷ is a hydrogen, alkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, hydroxy, hydroxyalkyl, thiol, alkylthiol, alkylsulfinyl, alkylsulfonyl, alkoxy, alkoxyalkyl, cyano, azido, nitro, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl radical;

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preferably, R' is a hydrogen, C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl or 1-3 halo radicals, C₁-C₄ haloalkoxy of 1-3 halo radicals, C₁-C₄ aminoalkyl, (C₁-C₄ alkyl)amino-C₁-C₄ alkyl, di(C₁-C₄ alkyl)amino-C₁-C₄ alkyl, aminosulfonyl, C₁-C₄ alkylaminosulfonyl, di(C₁-C₄ alkyl)aminosulfonyl, hydroxy, C₁-C₄ hydroxyalkyl, thiol, C₁-C₄ alkylthiol, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, C₁-C₄ alkoxy, (C₁-C₄ alkoxy)C₁-C₄ alkyl, cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical;

more preferably, R^7 is a hydrogen, C_1-C_4 alkyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, C_1-C_4 hydroxyalkyl, C_1-C_4 alkoxy, carboxy, $(C_1-C_4$ alkoxy)carbonyl, aminocarbonyl, $(C_1-C_4$ alkyl)aminocarbonyl or di(C_1-C_4 alkyl)aminocarbonyl radical;

more preferably, R¹ is a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, methoxy or ethoxy radical; most preferably, R¹ is a hydrogen radical.

The compounds of this invention may have in general several asymmetric centers and are typically depicted in the form of racemic mixtures. This invention is intended to encompass racemic mixtures, partially racemic mixtures and separate enantiomers and diastereomers.

Compounds of interest include the following:

2-cyclohexyloxy-5-(2-chlorophenylcarbonylamino)pyridine;
2-cyclohexyloxy-5-(2-methylphenylcarbonylamino)pyridine;

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- 2-(cyclohexyloxy)-5-(2,6-dichlorophenylcarbonylamino)
pyridine;
2-cyclohexyloxy-5-(2,6-dimethylphenylcarbonylamino)
pyridine;
- 2-(2,4-dimethylphenoxy)-5-(2-chlorophenylcarbonylamino)
pyridine;
2-(2,4-dimethylphenoxy)-5-(2,6-dichlorophenylcarbonyl
amino) pyridine;
2-(2,4-dimethylphenoxy)-5-(2-methylphenyl carbonylamino)
pyridine;
- 2-(2,6-dimethyl-4-chlorophenoxy)-5-(2,6-dimethylphenyl
carbonylamino) pyridine;
2-(2-methyl-4-fluorophenoxy)-5-(2-methylphenylcarbonyl
amino) pyridine;
- 2-(2-methyl-4-chlorophenoxy)-5-(2-chlorophenylcarbonyl
amino) pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2-methylphenylcarbonyl
amino) pyridine;
2-(2-methylphenoxy)-5-(2-chlorophenylcarbonylamino)
pyridine;
- 2-(2-methylphenoxy)-5-(2,6-dichlorophenyl
carbonylamino) pyridine;
2-(2-methylphenoxy)-5-(2-methylphenylcarbonyl
amino) pyridine;
- 2-(2-methyl-4-chlorophenoxy)-5-(2,6-dichlorophenyl
carbonylamino) pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2,6-dimethylphenyl
carbonylamino) pyridine;
2-(4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylami no)
pyridine;
- 2-(2-methyl-4-fluorophenoxy)-5-(2,6-dichlorophenyl
carbonylamino) pyridine;
2-(2-methyl-4-fluorophenoxy)-5-(2,6-dimethylphenyl
carbonylamino) pyridine;
2-(2-methylphenoxy)-5-(2,6-dimethylphenyl
carbonylamino) pyridine;

- 2-(2-methyl-4-fluorophenoxy)-5-(2-fluorophenylcarbonyl amino)pyridine;
 2-(2,4-dimethylphenoxy)-5-(2,6-dimethylphenylcarbonyl amino)pyridine;
 5 2-(1-naphthyl-4-fluorophenoxy)-5-(2-methylphenylcarbonylamino) pyridine;
 2-(1-naphthyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino) pyridine;
 2-(1-naphthyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino) pyridine;
 10 2-(1-naphthyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino) pyridine;
 2-(2-methyl-3-pyridyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonyl amino)pyridine;
 2-(2-methyl-4-chlorophenoxy)-5-(3,5-dimethyl-4-isoxazolyl)carbonylamino)pyridine;
 15 2-(2-methyl-4-chlorophenylthiol)-5-(2-methylphenylcarbonyl amino)pyridine;
 2-(2-methyl-4-chlorophenylthiol)-5-(2,6-dimethylphenylcarbonyl amino)pyridine;
 2-cyclohexylamino-5-(2,6-dichlorophenylcarbonylamino) pyridine;
 20 2-cyclohexylamino-5-(2,6-dimethylphenylcarbonylamino) pyridine;
 2-(2-methylcyclohexylamino)-5-(2,6-dichlorophenylcarbonyl amino)pyridine;
 25 2-(2-methylcyclohexylamino)-5-(2-methylphenylcarbonyl amino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2-fluorophenylcarbonyl amino)pyridine;
 30 2-(2,4-dimethylphenylamino)-5-(2-chlorophenylcarbonyl amino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2,6-dichlorophenylcarbonyl amino)pyridine;
 2-(2-methyl-4-chlorophenylamino)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
 35 2-(2,4-dimethylphenylamino)-5-(2-methylphenylcarbonyl amino)pyridine;

- 2-(2-methylphenylamino)-5-(2-methylphenylcarbonyl amino)pyridine;
 2-(2-methylphenylamino)-5-(2,6-dichlorophenylcarbonyl amino)pyridine;
 5 2-(2-methylphenylamino)-5-(2,6-dimethylphenylcarbonyl amino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2,6-dimethylphenylcarbonyl amino)pyridine;
 2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenyl carbonylamino)pyridine;
 10 2-(2-methyl-4-chlorophenylamino)-5-(2,6-dimethylphenyl carbonylamino)pyridine; and
 2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenyl aminocarbonyl)pyridine.

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As utilized herein, the following terms shall have the following meanings:

- "Alkyl", alone or in combination, means a straight-chain or branched-chain alkyl radical containing preferably 1-15 carbon atoms (C₁-C₁₅), more preferably 1-8 carbon atoms (C₁-C₈), even more preferably 1-6 carbon atoms (C₁-C₆), yet more preferably 1-4 carbon atoms (C₁-C₄), still more preferably 1-3 carbon atoms (C₁-C₃), and most preferably 1-2 carbon atoms (C₁-C₂). Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isomethyl, hexyl, octyl and the like.
- 30 "Hydroxyalkyl", alone or in combination, means an alkyl radical as defined above wherein at least one hydrogen radical is replaced with a hydroxyl radical, preferably 1-3 hydrogen radicals are replaced by hydroxyl radicals, more preferably 1-2 hydrogen radicals are replaced by hydroxyl radicals, and most preferably one hydrogen radical is replaced by a hydroxyl radical. Examples of such radicals include hydroxymethyl, 1-, 2-hydroxyethyl,
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1-, 2-, 3-hydroxypropyl, 1,3-dihydroxy-2-propyl, 1,3-dihydroxybutyl, 1,2,3,4,5,6-hexahydroxy-2-hexyl and the like.

5 "Alkenyl", alone or in combination, means a straight-chain or branched-chain hydrocarbon radical having one or more double bonds, preferably 1-2 double bonds and more preferably one double bond, and containing preferably 2-15 carbon atoms (C₂-C₁₅), more preferably 2-8 carbon atoms (C₂-C₈), even more preferably 2-4 carbon atoms (C₂-C₄), and still more preferably 2-3 carbon atoms (C₂-C₃). Examples of such alkenyl radicals include ethenyl, propenyl, 2-methylpropenyl, 1,4-butadienyl and the like.

15 "Alkoxy", alone or in combination, means a radical of the type "R-O-" wherein "R" is an alkyl radical as defined above and "O" is an oxygen atom. Examples of such alkoxy radicals include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy and the like.

20 "Alkoxycarbonyl", alone or in combination, means a radical of the type "R-O-C(O)-" wherein "R-O-" is an alkoxy radical as defined above and "C(O)" is a carbonyl radical.

25 "Alkoxycarbonylamino", alone or in combination, means a radical of the type "R-O-C(O)-NH-" wherein "R-O-C(O)" is an alkoxycarbonyl radical as defined above, wherein the amino radical may optionally be substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl and the like.

30 "Alkylthio", alone or in combination, means a radical of the type "R-S-" wherein "R" is an alkyl radical as

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defined above and "S" is a sulfur atom. Examples of such alkylthio radicals include methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, iso-butylthio, sec-butylthio, tert-butylthio and the like.

5 "Alkylsulfinyl", alone or in combination, means a radical of the type "R-S(O)-" wherein "R" is an alkyl radical as defined above and "S(O)" is a mono-oxygenated sulfur atom. Examples of such alkylsulfinyl radicals include methylsulfinyl, ethylsulfinyl, n-propylsulfinyl, isopropylsulfinyl, n-butylsulfinyl, iso-butylsulfinyl, sec-butylsulfinyl, tert-butylsulfinyl and the like.

10 "Alkylsulfonyl", alone or in combination, means a radical of the type "R-S(O)₂-" wherein "R" is an alkyl radical as defined above and "S(O)₂" is a di-oxygenated sulfur atom. Examples of such alkylsulfonyl radicals include methylsulfonyl, ethylsulfonyl, n-propylsulfonyl, isopropylsulfonyl, n-butylsulfonyl, iso-butylsulfonyl, sec-butylsulfonyl, tert-butylsulfonyl and the like.

15 "Aryl", alone or in combination, means a phenyl or biphenyl radical, which is optionally benzo fused or heterocyclo fused and which is optionally substituted with one or more substituents selected from alkyl, alkoxy, halogen, hydroxy, amino, azido, nitro, cyano, haloalkyl, carboxy, alkoxycarbonyl, cycloalkyl, alkanoylamino, amido, amidino, alkoxycarbonylamino, N-alkylamidino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, N-alkylamido, N,N-dialkylamido, aralkoxycarbonylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, oxo and the like.

20 Examples of aryl radicals are phenyl, o-tolyl, 4-methoxyphenyl, 2-(tert-butoxy)phenyl, 3-methyl-4-methoxyphenyl, 2-CF₃-phenyl, 2-fluorophenyl, 2-methoxyphenyl, 2-nitrophenyl, 3-aminophenyl, 3-chlorophenyl, 3-nitrophenyl, 3-aminophenyl, 6-acetamidophenyl, 2-amino-3-(aminomethyl)phenyl, 6-

methyl-3-acetamidophenyl, 6-methyl-2-aminophenyl, 6-methyl-2,3-diaminophenyl, 2-amino-3-methylphenyl, 4,6-dimethyl-2-aminophenyl, 4-hydroxyphenyl, 3-methyl-4-hydroxyphenyl, 4-(2-methoxyphenyl)phenyl, 2-amino-1-naphthyl, 2-naphthyl, 3-amino-2-naphthyl, 1-methyl-3-amino-2-naphthyl, 2,3-diamino-1-naphthyl, 4,8-dimethoxy-2-naphthyl and the like.

"Arylalkyl" and "arylalkyl", alone or in combination,

means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by an aryl radical as defined above, such as benzyl, 1-, 2-phenylethyl, dibenzylmethyl, hydroxyphenylmethyl, methylphenylmethyl, diphenylmethyl, dichlorophenylmethyl, 4-methoxyphenylmethyl and the like.

"Alkoxy", alone or in combination, means an alkoxy radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by an aryl radical as defined above, such as benzyloxy, 1-, 2-phenylethoxy, dibenzylmethoxy, hydroxyphenylmethoxy, methylphenylmethoxy, dichlorophenylmethoxy, 4-methoxyphenylmethoxy and the like.

"Alkoxycarbonyl", alone or in combination, means a radical of the type "R-O-C(O)-" wherein "R-O-" is an alkoxy radical as defined above and "-C(O)-" is a carbonyl radical.

"Alkanoyl", alone or in combination, means a radical of the type "R-C(O)-" wherein "R" is an alkyl radical as defined above and "-C(O)-" is a carbonyl radical.

Examples of such alkanoyl radicals include acetyl, trifluoroacetyl, hydroxyacetyl, propionyl, butyryl, valeryl, 4-methylvaleryl, and the like.

"Alkanoylamino", alone or in combination, means a radical of the type "R-C(O)-NH-" wherein "R-C(O)-" is an alkanoyl radical as defined above, wherein the amino radical may optionally be substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl and the like.

"Aminocarbonyl", alone or in combination, means an amino substituted carbonyl (carbamoyl) radical, wherein the amino radical may optionally be mono- or di-substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, alkanoyl, alkoxy carbonyl, aralkoxy carbonyl and the like.

"Aminosulfonyl", alone or in combination, means an amino substituted sulfonyl radical.

"Benzo", alone or in combination, means the divalent radical C₆H₄= derived from benzene. "Benzo fused" forms a ring system in which benzene and a cycloalkyl or aryl group have two carbons in common, for example tetrahydronaphthylene and the like.

"Bicyclic" as used herein is intended to include both fused ring systems, such as naphthyl and 8-carbolinyl, and substituted ring systems, such as biphenyl, phenylpyridyl and diphenylpiperazinyl.

"Cycloalkyl", alone or in combination, means a saturated or partially saturated, preferably one double bond, monocyclic, bicyclic or tricyclic carbocyclic alkyl radical, preferably monocyclic, containing preferably 5-12 carbon atoms (C₅-C₁₂), more preferably 5-10 carbon atoms (C₅-C₁₀), even more preferably 5-7 carbon atoms (C₅-C₇), which is optionally benzo fused or heterocyclo fused and which is optionally substituted as defined herein with respect to the definition of aryl. Examples

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of such cycloalkyl radicals include cyclopentyl, cyclohexyl, dihydroxycyclohexyl, ethylenedioxcyclohexyl, cycloheptyl, octahydronaphthyl, tetrahydronaphthyl, octahydroquinolinyl, dimethoxytetrahydronaphthyl, 2,3-dihydro-1H-indenyl, azabicyclo[3.2.1]octyl and the like.

"Heteroatoms" means nitrogen, oxygen and sulfur heteroatoms.

"Heterocyclo fused" forms a ring system in which a heterocyclyl or heteroaryl group of 5-6 ring members and a cycloalkyl or aryl group have two carbons in common, for example indole, isouquinoline, tetrahydroquinoline, methylenedioxybenzene and the like.

"Heterocyclyl" means a saturated or partially unsaturated, preferably one double bond, monocyclic or bicyclic, preferably monocyclic, heterocycle radical containing at least one, preferably 1 to 4, more preferably 1 to 3, even more preferably 1-2, nitrogen, oxygen or sulfur atom ring member and having preferably 3-8 ring members in each ring, more preferably 5-8 ring members in each ring and even more preferably 5-6 ring members in each ring. "Heterocyclyl" is intended to include sulfone and sulfoxide derivatives of sulfur ring members and N-oxides of tertiary nitrogen ring members, and carbocyclic fused, preferably 3-6 ring carbon atoms and more preferably 5-6 ring carbon atoms, and benzo fused ring systems. "Heterocyclyl" radicals may optionally be substituted on at least one, preferably 1-4, more preferably 1-3, even more preferably 1-2, carbon atoms by halogen, alkyl, alkoxy, hydroxy, oxo, thio, aryl, aralkyl, heteroaryl, heteroaralkyl, amidino, N-alkylamidino, alkoxy-carbonylamino, alkylsulfonylamino and the like, and/or on a secondary nitrogen atom by hydroxy, alkyl, aralkoxy-carbonyl, alkanoyl,

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alkoxy-carbonyl, heteroaralkyl, aryl or aralkyl radicals. More preferably, "heterocyclyl", alone or in combination, is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thio radicals. Examples of such heterocyclyl radicals include pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl and its sulfoxide and sulfone derivatives, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisouquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isouquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl, ethylenedioxyphenyl and the like.

"Heteroaryl" means a monocyclic or bicyclic, preferably monocyclic, aromatic heterocycle radical, having at least one, preferably 1 to 4, more preferably 1 to 3, even more preferably 1-2, nitrogen, oxygen or sulfur atom ring members and having preferably 5-6 ring members in each ring, which is optionally saturated carbocyclic fused, preferably 3-4 carbon atoms (C₃-C₄) to form 5-6 ring membered rings and which is optionally substituted as defined above with respect to the definitions of aryl. Examples of such heteroaryl groups include imidazolyl, 1-benzoyloxy-carbonylimidazol-4-yl, pyrrolyl, pyrazolyl, pyridyl, 3-(2-methyl)pyridyl, 3-(4-trifluoromethyl)pyridyl, pyrimidinyl, 5-(4-trifluoromethyl)pyrimidinyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, 5,6,7,8-tetrahydroquinolinyl, 5,6,7,8-tetrahydroisouquinolinyl, quinoxalinyl, benzothiazolyl, benzofuryl, benzimidazolyl, benzoxazolyl and the like.

"Heteroalkyl" and "heteroarylalkyl," alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by a heteroaryl radical as defined above, such as 3-furylpropyl, 2-pyrrolyl propyl, chloroquinolinylmethyl, 2-thienylethyl, pyridylmethyl, 1-imidazolylethyl and the like.

10 "Halogen" and "halo", alone or in combination, means fluoro, chloro, bromo or iodo radicals.

"Haloalkyl", alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-3, is replaced by a halogen radical, more preferably fluoro or chloro radicals. Examples of such haloalkyl radicals include 1,1,1-trifluoroethyl, chloromethyl, 1-bromoethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 20 bis(trifluoromethyl)methyl and the like.

"Pharmacologically acceptable salt" means a salt prepared by conventional means, and are well known by those skilled in the art. The "pharmacologically acceptable salts" include basic salts of inorganic and organic acids, including but not limited to hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, ethanesulfonic acid, malic acid, acetic acid, oxalic acid, tartaric acid, citric acid, lactic acid, fumaric acid, succinic acid, maleic acid, salicylic acid, benzoic acid, phenylacetic acid, mandelic acid and the like. When compounds of the invention include an acidic function such as a carboxy group, then suitable pharmaceutically acceptable cation pairs for the carboxy group are well known to those skilled in the art and include alkaline, alkaline earth, ammonium, quaternary ammonium cations and the like. For

additional examples of "pharmacologically acceptable salts," see *infra* and Berge et al, *J. Pharm. Sci.* 66, 1 (1977).

5 "Cytokine" means a secreted protein that affects the functions of other cells, particularly as it relates to the modulation of interactions between cells of the immune system or cells involved in the inflammatory response. Examples of cytokines include but are not limited to interleukin 1 (IL-1), preferably IL-18, interleukin 6 (IL-6), interleukin 8 (IL-8) and TNF, preferably TNF- α (tumor necrosis factor- α).

"TNF, IL-1, IL-6, and/or IL-8 mediated disease or disease state" means all disease states wherein TNF, IL-1, IL-6, and/or IL-8 plays a role, either directly as TNF, IL-1, IL-6, and/or IL-8 itself, or by TNF, IL-1, IL-6, and/or IL-8 inducing another cytokine to be released. For example, a disease state in which IL-1 plays a major role, but in which the production of or action of IL-1 is a result of TNF, would be considered mediated by TNF.

25 "Leaving group" generally refers to groups readily displaceable by a nucleophile, such as an amine, a thiol or an alcohol nucleophile. Such leaving groups are well known in the art. Examples of such leaving groups include, but are not limited to, N-hydroxysuccinimide, N-hydroxybenzotriazole, halides, triflates, tosylates and the like. Preferred leaving groups are indicated herein where appropriate.

30 "Protecting group" generally refers to groups well known in the art which are used to prevent selected reactive groups, such as carboxy, amino, hydroxy, mercapto and the like, from undergoing undesired reactions, such as nucleophilic, electrophilic, oxidation, reduction and the

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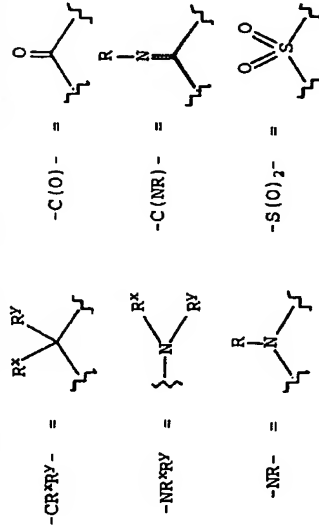
like. Preferred protecting groups are indicated herein where appropriate. Examples of amino protecting groups include, but are not limited to, aralkyl, substituted aralkyl, cycloalkenylalkyl and substituted cycloalkenyl alkyl, allyl, substituted allyl, acyl, alkoxy carbonyl, aralkoxy carbonyl, silyl and the like. Examples of aralkyl include, but are not limited to, benzyl, ortho-methylbenzyl, trityl and benzhydryl, which can be optionally substituted with halogen, alkyl, alkoxy, hydroxy, nitro, acylamino, acyl and the like, and salts, such as phosphonium and ammonium salts. Examples of aryl groups include phenyl, naphthyl, indanyl, anthracenyl, 9-(9-phenylfluorenyl), phenanthrenyl, durenyl and the like. Examples of cycloalkenylalkyl or substituted cycloalkenylalkyl radicals, preferably have 6-10 carbon atoms, include, but are not limited to, cyclohexenyl methyl and the like. Suitable acyl, alkoxy carbonyl and aralkoxy carbonyl groups include benzyloxy carbonyl, t-butoxycarbonyl, iso-butoxycarbonyl, benzoyl, substituted benzoyl, butyryl, acetyl, tri-fluoroacetyl, tri-chloro acetyl, phthaloyl and the like. A mixture of protecting groups can be used to protect the same amino group, such as a primary amino group can be protected by both an aralkyl group and an aralkoxy carbonyl group. Amino protecting groups can also form a heterocyclic ring with the nitrogen to which they are attached, for example, 1,2-bis(methylene)benzene, phthalimideyl, succinimideyl, maleimideyl and the like and where these heterocyclic groups can further include adjoining aryl and cycloalkyl rings. In addition, the heterocyclic groups can be mono-, di- or tri-substituted, such as nitrophthalimideyl. Amino groups may also be protected against undesired reactions, such as oxidation, through the formation of an addition salt, such as hydrochloride, toluenesulfonic acid, trifluoroacetic acid and the like. Many of the amino protecting groups are also suitable for protecting carboxy, hydroxy and mercapto groups. For example,

32

aralkyl groups. Alkyl groups are also suitable groups for protecting hydroxy and mercapto groups, such as tert-butyl. Silyl protecting groups are silicon atoms optionally substituted by one or more alkyl, aryl and aralkyl groups. Suitable silyl protecting groups include, but are not limited to, trimethylsilyl, triethylsilyl, tri-isopropylsilyl, tert-butyl dimethylsilyl, dimethylphenylsilyl, 1,2-bis(dimethylsilyl)benzene, 1,2-bis(dimethylsilyl)ethane and diphenylmethylsilyl. Silylation of an amino groups provide mono- or di-silylamino groups. Silylation of aminoalcohol compounds can lead to a N,N,O-tri-silyl derivative. Removal of the silyl function from a silyl ether function is readily accomplished by treatment with, for example, a metal hydroxide or ammonium fluoride reagent, either as a discrete reaction step or in situ during a reaction with the alcohol group. Suitable silylating agents are, for example, trimethylsilyl chloride, tert-butyl-dimethylsilyl chloride, phenyldimethylsilyl chloride, diphenylmethylsilyl chloride or their combination products with imidazole or DMF. Methods for silylation of amines and removal of silyl protecting groups are well known to those skilled in the art. Methods of preparation of these amine derivatives from corresponding amino acids, amino acid amides or amino acid esters are also well known to those skilled in the art of organic chemistry including amino acid/amino acid ester or aminoalcohol chemistry. Protecting groups are removed under conditions which will not affect the remaining portion of the molecule. These methods are well known in the art and include acid hydrolysis, hydrogenolysis and the like. A preferred method involves removal of a protecting group, such as removal of a benzyloxy carbonyl group by hydrogenolysis utilizing palladium on carbon in a

5 suitable solvent system such as an alcohol, acetic acid, and the like or mixtures thereof. A t-butoxycarbonyl protecting group can be removed utilizing an inorganic or organic acid, such as HCl or trifluoroacetic acid, in a suitable solvent system, such as dioxane or methylene chloride. The resulting amino salt can readily be neutralized to yield the free amine. Carboxy protecting group, such as methyl, ethyl, benzyl, tert-butyl, 4-methoxyphenylmethyl and the like, can be removed under hydrolysis and hydrogenolysis conditions well known to those skilled in the art.

The symbols used above have the following meanings:



15 Procedures for preparing the compounds of this invention are set forth below. It should be noted that the general procedures are shown as it relates to preparation of compounds having unspecified stereochemistry. However, such procedures are generally applicable to those compounds of a specific stereochemistry, e.g., where the stereochemistry about a group is (S) or (R). In addition, the compounds having one stereochemistry (e.g., (R)) can often be utilized to produce those having opposite stereochemistry (i.e., (S)) using well-known methods, for example, by inversion.

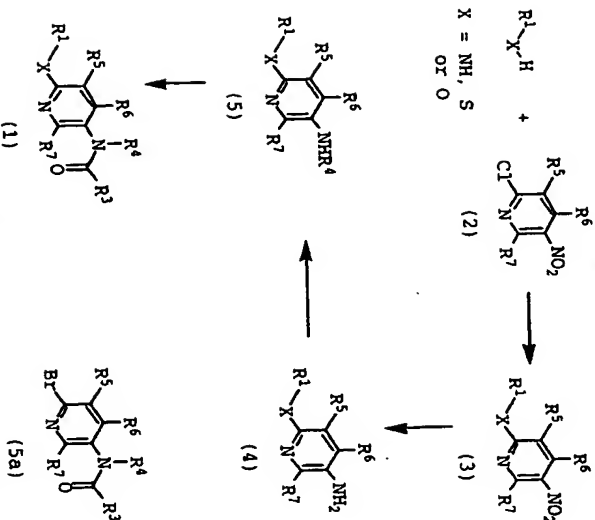
Preparation of Compounds of Formula I

5 The compounds of the present invention represented by Formula I above can be prepared utilizing the following general procedures. Hetero-aromatic Nitrogen Compounds, Pyroles and Pyrrolines: Schofield, Kenneth; Plenum Press, New York, NY; (1967) and Advances in Nitrogen Heterocycles: JAI Press, Greenwich, CN; (1995) describe procedures and references that may be useful in preparing compounds of the present invention.

2-Halo-5-nitro-pyridine analogs (2) can be treated with the appropriate amine, alcohol, phenol, or thiol (R'-X-H) in the presence of base or Cu(I) in an appropriate solvent, such as THF, DMF, DME, DMSO and the like, at a temperature from -20°C to 120°C to form 2-substituted-5-nitropyridines (3) (Scheme I). Reduction of the nitro group can be performed by treatment of (3) with hydrogen gas in the presence of palladium on carbon or Raney nickel, or alternatively, by treatment with SnCl₄ in an alcoholic solvent and in the presence or absence of HCl to obtain 2-substituted-5-aminopyridines (4). The aminopyridines (4) may be alkylated using alkylhalides and an appropriate base or by reductive alkylation employing the appropriate aldehyde or ketone in the presence of a reducing agent, such as sodium triacetoxy borohydride, borane-THF and the like, to form the substituted aminopyridines (5). Either (4) or (5) may be acylated with an appropriate acid halide (e.g., R'C(O)Cl or R'C(O)Br) in the presence of a base, such as pyridine, DMAP and the like, or alternatively may be acylated with an anhydride, either mixed or symmetrical, or alternatively may be acylated by treatment with the appropriate acid (R'CO₂H) in the presence of a coupling agent such as a carbodiimide reagent to form the final product (1). Alternatively, substituted 2-bromo-5-nitropyridine analogs may be reduced to, substituted 2-

bromo-5-aminopyridine analogs by the action of SnBr_4 in methanolic solvent. Subsequent acylation with an appropriate activated ester (i.e.: $\text{R}'\text{CO}_2\text{H}$ in the presence of diisopropylcarbodiimide in methylene chloride as solvent) produces 2-bromopyridine-5-carboxamide compounds of structure (5a). Coupling of (5a) with an appropriate phenol in the presence of $\text{Cu}(\text{Ac})_2$ and K_2CO_3 in DMF at 140°C provides compounds of formula (1) where $\text{X} = \text{O}$.

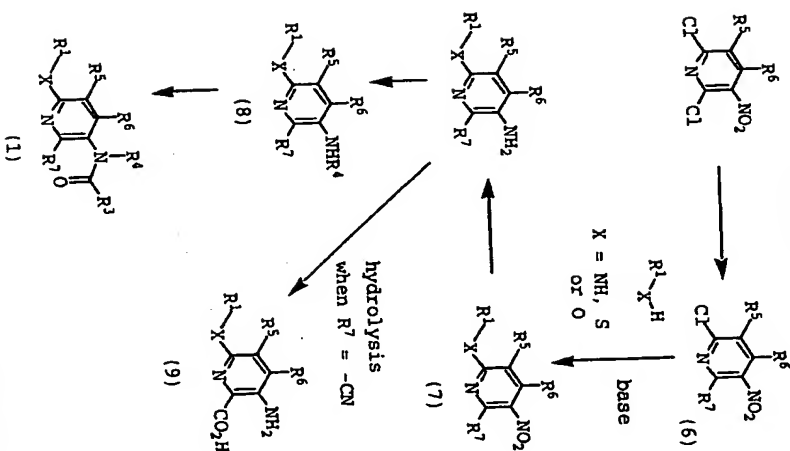
SCHEME I



6-Substituted-2-halo-5-nitro-pyridine analogs (6) may be prepared from 2,6-dichloro-5-nitropyridine according to the methods outlined in Scheme II. Treatment with one equivalent of an appropriate nucleophile of R' or a precursor thereof (such as, HO^- , RO^- , AcS^- , NC^- , RS^- and the like) provides (6). Subsequent reaction to form (7) (treatment with $\text{R}^1\text{-X-H}$

in the presence of base or $\text{Cu}(\text{I})$ in an appropriate solvent, such as THF, DMF, DME, DMSO and the like, at a temperature from -20°C to 120°C) and (8) (reduction of the nitro group and substitution with R^1) is as described in Scheme I (cf. Colbry, N.L. et al.; J. Heterocyclic Chem., 21: 1521-1525 (1984); Matsumoto, Jun-ichi, et al.; J. Heterocyclic Chem., 21: 673-679 (1984)). (8) may be reacted with an acid halide or an activated

SCHEME II



ester as shown in Scheme I to provide compounds of formula (1). Where $\text{R}^1 = \text{CN}$, compounds of formula (8)

may be hydrolyzed to acids ($R' = CO_2H$) of formula (9) using acidic media such as HBr and the like. Utilizing the appropriate N-protecting groups, acids of formula (9) may be transformed into esters, amides and alcohols.

Compounds of formula (9) and derivatives described above may be reacted with an acid halide or an activated ester as shown in Scheme I to provide compounds of formula (1). Compounds of formula (8), where $R' = -CN$, may be reduced to the primary amine ($R' = -CH_2NH_2$) using reagents such as BH_3 or hydrogen gas in the presence of palladium on carbon or Raney nickel. Subsequent manipulation and reaction of the primary amine may be performed in the presence of the pyridine-5-amine substituent due to its greater reactivity.

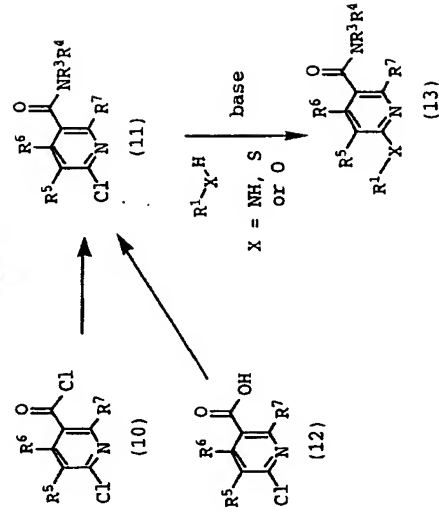
Specifically, compounds of formula (8) where $R' = -CH_2NH_2$, may be alkylated by treatment with an appropriate aldehyde or ketone in the presence of a reducing agent, such as sodium triacetoxy borohydride, or may be acylated by treatment with an appropriate activated ester, chloroformate, isocyanate and the like, or may be sulfonylated by treatment with an appropriate sulfonyl halide. Alternatively, substituted 3-aminopyridine intermediates may be prepared from the corresponding nicotinamide compound using Hofmann's reaction.

When R' and/or R'' is an alkyl group, such as methyl, in compound (7), containing the appropriate protecting groups of or avoiding the presence of base sensitive groups, can be treated with strong base such as $NaNH_2$, $PhLi$, NaH or the like at temperatures from $-78^\circ C$ to $22^\circ C$ then treated with electrophiles, such as alkyl halides, aldehydes, ketones and the like (cf. Fuerst, Feustel; CHEMTECH; 10: 693-699 (1958); Nishigaki, S. et al.; Chem. Pharm. Bull.; 17: 1827-1831 (1969); Kaiser, Edwin M.; Tetrahedron; 39: 2055-2064 (1983)). Alternatively, the alkyl group may be halogenated and the haloalkyl group may be reacted with a nucleophile, such as an amino group, alkoxy, alkylthiol and the like.

6-Chloronicotinoyl chloride analogs (10) are treated with the appropriate amine (R^3R^4NH) in the presence of base in an appropriate solvent, such as dichloromethane, acetonitrile, DMF, THF and the like, at a temperature from $-20^\circ C$ to $120^\circ C$ to form nicotinamides (11) as shown in Scheme III. Alternatively, 6-chloronicotinic acid analogs (12) may be coupled with the appropriate amine via an anhydride, either mixed or symmetrical, or alternatively by treatment with the appropriate amine in the presence of a coupling agent such as a carbodiimide reagent to form the amide (11).

6-Chloronicotinamide analogs (11) are treated with the appropriate R^1-X-H in the presence of absence of base, or $Cu(I)$ in an appropriate solvent, such as pyridine, ethylene glycol, DMF, DME, DMSO and the like, at a temperature from $-20^\circ C$ to $180^\circ C$ to form the final product (13).

SCHEME III



Substituted halopyridines may be readily prepared from the corresponding pyridones using phosphorus oxychloride or pentachloride.

39

Amines of formula NR^1R^2 and NR^1R^2 are commercially available or can be readily prepared by those skilled in the art from commercially available starting materials.

For example, an amide, nitro or cyano group can be

reduced under reducing conditions, such as in the presence of a reducing agent like lithium aluminum hydride and the like, to form the corresponding amine.

Alkylation and acylation of amino groups are well known in the art. Chiral and achiral substituted amines can

be prepared from chiral amino acids and amino acid

amides (for example, alkyl, aryl, heteroaryl,

cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl

and the like) using methods well known in the art, such

as H. Brunner, P. Hankofer, U. Holzinger, B. Treitinger

and H. Schoenenberger, Eur. J. Med. Chem. 25, 35-44,

1990; M. Preiberger and R. B. Hasbrouck, J. Am. Chem.

Soc. 82, 696-698, 1960; Dornow and Fust, Chem. Ber. 87,

984, 1954; M. Kojima and J. Fujita, Bull. Chem. Soc.

Jpn. 55, 1454-1459, 1982; W. Wheeler and D. O'Bannon,

Journal of Labelled Compounds and Radiopharmaceuticals

XXXI, 306, 1992; and S. Davies, N. Garrido, O. Ichihara

and I. Walters, J. Chem. Soc., Chem. Commun. 1153, 1993.

Alkyl sulfonic acids, aryl sulfonic acids,

heterocyclyl sulfonic acids, heteroaryl sulfonic acids,

alkylmercaptans, arylmercaptans, heterocyclylmercaptans,

heteroarylmercaptans, alkylhalides, arylhalides,

heterocyclylhalides, heteroarylhalides, and the like are

commercially available or can be readily prepared from

starting materials commercially available using standard

methods well known in the art.

Thioether derivatives can be converted into the

corresponding sulfone or sulfoxide by oxidizing the

thioether derivative with a suitable oxidation agent in

a suitable solvent. Suitable oxidation agents include,

for example, hydrogen peroxide, sodium meta-perborate,

oxone (potassium peroxy monosulfate), meta-

chloroperoxybenzoic acid, periodic acid and the like,

including mixtures thereof. Suitable solvents include acetic acid (for sodium meta-perborate) and, for other peracids, ethers such as THF and dioxane, and acetonitrile, DMF and the like, including mixtures thereof.

The chemical reactions described above are

generally disclosed in terms of their broadest

application to the preparation of the compounds of this

invention. Occasionally, the reactions may not be

applicable as described to each compound included within

the disclosed scope. The compounds for which this

occurs will be readily recognized by those skilled in

the art. In all such cases, either the reactions can be

successfully performed by conventional modifications

known to those skilled in the art, e.g., by appropriate

protection of interfering groups, by changing to

alternative conventional reagents, by routine

modification of reaction conditions, and the like, or

other reactions disclosed herein or otherwise

conventional, will be applicable to the preparation of

the corresponding compounds of this invention. In all

preparative methods, all starting materials are known or

readily prepared from known starting materials.

Prodrugs of the compounds of this invention are

also contemplated by this invention. A prodrug is an

active or inactive compound that is modified chemically

through in vivo physiological action, such as

hydrolysis, metabolism and the like, into a compound of

this invention following administration of the prodrug to

a patient. The suitability and techniques involved in

making and using prodrugs are well known by those

skilled in the art. For a general discussion of

prodrugs involving esters see Svensson and Tunek Drug

Metabolism Reviews 165 (1988) and Bundgaard Design of

Prodrugs, Elsevier (1985). Examples of a masked

carboxylate anion include a variety of esters, such as

alkyl (for example, methyl, ethyl), cycloalkyl (for

example, methyl, ethyl), cycloalkyl (for

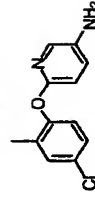
example, cyclohexyl), aralkyl (for example, benzyl, p-methoxybenzyl), and alkylcarbonyloxyalkyl (for example, pivaloyloxymethyl). Amines have been masked as arylcarbonyloxymethyl substituted derivatives which are cleaved by esterases in vivo releasing the free drug and formaldehyde (Bungaard J. Med. Chem. 2503 (1989)).

Also, drugs containing an acidic NH group, such as imidazole, imide, indole and the like, have been masked with N-acyloxymethyl groups (Bundgaard Design of Prodrugs, Elsevier (1985)). Hydroxy groups have been masked as esters and ethers. EP 039,051 (Sloan and Little, 4/11/81) discloses Mannich-base hydroxamic acid prodrugs, their preparation and use.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. The following Examples illustrate the preparation of compounds of the present invention and intermediates useful in preparing the compounds of the present invention.

25

Example 1



Preparation of 2-(4-Chloro-2-methylphenoxy)-5-amino-pyridine

30

Step A. 2-(4-Chloro-2-methylphenoxy)-5-nitropyridine 4-Chloro-2-methylphenol (101 mg, 0.71 mmol) was dissolved in tetrahydrofuran (2.1 mL) and the solution was treated with sodium hydride (60% dispersed in mineral oil, 31 mg, 0.78 mmol). After stirring for 30

minutes at 22°C, 2-chloro-5-nitropyridine (101 mg, 0.64 mmol) was added and the reaction mixture was heated to reflux for 1 hour. The solution was cooled to ambient temperature, quenched with saturated aqueous NH_4Cl and concentrated in *vacuo*. The residue was redissolved in ethyl acetate then washed 2x with saturated NaHCO_3 , saturated NaCl , dried over anhydrous Na_2SO_4 and concentrated in *vacuo*.

Step B: 2-(4-Chloro-2-methylphenoxy)-5-amino-pyridine 2-(4-chloro-2-methylphenoxy)-5-nitropyridine (203 mg, 0.77 mmol) was dissolved in 95% ethanol (3 mL) and treated with 20% palladium hydroxide on carbon (50 mg). The reaction mixture was shaken in a hydrogen atmosphere (40 psi) for 1 hour. The solution was filtered through celite and concentrated in *vacuo*. MS (m/z): 234/236 ($M+H$); $\text{C}_{11}\text{H}_{10}\text{N}_2\text{OCl}$ requires 234.7.

Example 2

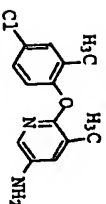
The compounds listed in Table 1 were prepared from 2-chloro-5-nitropyridine and the appropriate alcohol, amine or thiol in the same manner as 2-(4-Chloro-2-methylphenoxy)-5-amino-pyridine was prepared.

25

Table 1

	MS (m/z)
2-(4-Chloro-2-methylphenoxy)-5-amino-pyridine	235
2-(4-Chloro-2,6-dimethylphenoxy)-5-amino-pyridine	249
2-(2-Methyl-pyridin-3-yl-oxy)-5-amino-pyridine	201
2-(4-Fluoro-2-methylphenoxy)-5-amino-pyridine	218
2-(2-Isopropylphenoxy)-5-amino-pyridine	228
2-(1-Naphthyl-oxy)-5-amino-pyridine	236

2-(Cyclohexyloxy)-5-amino-pyridine	192
2-(2-Methylphenoxy)-5-amino-pyridine	200
2-(2,4-Dimethylphenoxy)-5-amino-pyridine	214
2-(4-Chlorophenoxy)-5-amino-pyridine	222
2-(Phenoxy)-5-amino-pyridine	186
2-(2-Methylcyclohexylamino)-5-amino-pyridine	205
2-(Cyclohexylamino)-5-amino-pyridine	191
2-(2-Methylanilino)-5-amino-pyridine	199
2-(4-Chloro-2-methylanilino)-5-amino-pyridine	233
2-(2,4-Dimethylanilino)-5-amino-pyridine	212
2-(4-Chloro-2-methylthiophenoxy)-5-amino-pyridine	251

Example 3

Preparation of 2-(4-Chloro-2-methyl-phenoxyl)-3-methyl-5-amino-pyridine

Step A: 2-(4-Chloro-2-methyl-phenoxyl)-3-methyl-5-nitropyridine

Sodium hydride (60% in mineral oil, 1.08 g, 27 mmol) was washed 3x with hexanes then a solution of 4-chloro-2-methylphenol (3.50 g, 24.5 mmol) dissolved in tetrahydrofuran (40 mL) was added. The solution was stirred for 20 minutes then 2-chloro-3-methyl-5-nitropyridine (4.02 g, 23.3 mmol) was added and the reaction mixture was heated to reflux for 3 hours. After cooling, the mixture was concentrated in vacuo then dissolved in ethyl acetate and washed with water, 3x with saturated NaHCO_3 and saturated NaCl then dried over Na_2SO_4 and concentrated in vacuo.

Step B: 2-(4-Chloro-2-methyl-phenoxyl)-3-methyl-5-amino-pyridine

2-(4-chloro-2-methyl-phenoxyl)-3-methyl-5-nitropyridine (5.8 g, 20.8 mmol) was dissolved in 95% ethanol (50 mL) and treated with 20% palladium hydroxide on carbon (350 mg). The reaction mixture was shaken in a hydrogen atmosphere (40 psi) for 1 hour. The solution was filtered through celite and concentrated in vacuo followed by chromatography on SiO_2 using 1:1 ethyl acetate / hexanes as eluant. MS (m/z): 248/250 (M^+H^+); $\text{C}_{14}\text{H}_{13}\text{N}_2\text{OCl}$ requires 248.7.

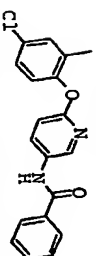
Example 4

The compounds listed in Table 2 were prepared from substituted 2-chloro-5-nitropyridine and 4-chloro-2-methylphenol in the same manner as 2-(4-Chloro-2-methyl-phenoxyl)-3-methyl-5-amino-pyridine was prepared.

20

Table 2

	MS (m/z)
2-(4-Chloro-2-methyl-phenoxyl)-4-methyl-5-amino-pyridine	249
6-(4-Chloro-2-methyl-phenoxyl)-2-methyl-3-amino-pyridine	249
6-(4-Chloro-2-methyl-phenoxyl)-2,3-diamino-pyridine	250

Example 5

Preparation of N-(2-(4-Chloro-2-methyl-phenoxyl)-pyridin-5-yl)-benzamide

25

2-(4-Chloro-2-methyl-phenoxy)-5-aminopyridine (211 mg, 0.90 mmol) was dissolved in methylene chloride (2.7 mL), then treated with triethylamine (0.19 mL, 1.35 mmol) followed by benzoyl chloride (0.13 mL, 1.12 mmol). The reaction mixture was stirred for 3 hours at 22°C then saturated aqueous NaHCO₃ was added and the mixture was stirred for another hour. The organic layer was separated and washed 2x with 6% aqueous NaHCO₃, dried over Na₂SO₄ and concentrated in vacuo. The residue was chromatographed on silica gel using 1:1 ethyl acetate / hexane as eluent. The product was recovered as a white solid. MS (m/z): 338/340 (M+H)⁺; C₁₄H₁₃N₃OCl requires 338.8.

15

Example 6

The compounds listed in Table 3 were prepared from substituted 5-aminopyridine compounds and the appropriate acid chloride in the same manner as N-(2-(4-Chloro-2-methyl-phenoxy)-pyridin-5-yl)-benzamide was prepared.

20

Table 3

	MS (m/z)
2-(4-Chloro-2-methyl-phenoxy)-5-(3-pyridyl)carbonylamino)pyridine	340
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dichlorophenyl)carbonylamino)pyridine	408
2-(4-Chloro-2-methyl-phenoxy)-5-(4-pyridyl)carbonylamino)pyridine	340
2-(4-Chloro-2-methyl-phenoxy)-5-((4-methoxyphenyl)carbonylamino)pyridine	369
2-(4-Chloro-2-methyl-phenoxy)-5-((4-pentylphenyl)carbonylamino)pyridine	409
2-(4-Chloro-2-methyl-phenoxy)-5-(2-naphthyl)carbonylamino)pyridine	389

2-(4-Chloro-2-methyl-phenoxy)-5-(2-thienyl)carbonylamino)pyridine	345
2-(4-Chloro-2-methyl-phenoxy)-5-((3,5-dimethyl-4-isoxazolyl)carbonylamino)pyridine	358
2-(4-Chloro-2-methyl-phenoxy)-5-((5-benzo[1,3]dioxol-yl)carbonylamino)pyridine	383
2-(4-Chloro-2-methyl-phenoxy)-5-((5-tert-butyl-2-methyl-2H-pyrazol-3-yl)carbonylamino)pyridine	399
2-(4-Chloro-2-methyl-phenoxy)-5-((2-benzo[b]thiophenyl)carbonylamino)pyridine	395
2-(4-Chloro-2-methyl-phenoxy)-5-((2-methoxyphenyl)carbonylamino)pyridine	369
2-(4-Chloro-2-methyl-phenoxy)-5-((3,5-dichlorophenyl)carbonylamino)pyridine	408
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dimethylphenyl)carbonylamino)pyridine	367
2-(4-Chloro-2-methyl-phenoxy)-5-((2-methylphenyl)carbonylamino)pyridine	353
2-(4-Chloro-2-methyl-phenoxy)-5-((2-nitrophenyl)carbonylamino)pyridine	384
2-(4-Chloro-2-methyl-phenoxy)-5-((2-acetoxyphenyl)carbonylamino)pyridine	397
2-(4-chloro-2,6-dimethylphenoxy)-5-((2,6-dichlorophenyl)carbonylamino)pyridine	422
2-(4-chloro-2,6-dimethylphenoxy)-5-((2,6-dimethylphenyl)carbonylamino)pyridine	381
2-(2-methyl-pyridin-3-yloxy)-5-((2,6-dichlorophenyl)carbonylamino)pyridine	374
2-(2-methyl-pyridin-3-yloxy)-5-((2,6-dimethylphenyl)carbonylamino)pyridine	333
2-(2-methyl-pyridin-3-yloxy)-5-((2-methylphenyl)carbonylamino)pyridine	319

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2-(4-fluoro-2-methylphenoxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	391		2-(2-methylphenoxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	332	
2-(4-fluoro-2-methylphenoxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	350		2-(2-methylphenoxy)-5-((12-chlorophenyl)carbonylamino)pyridine	339	
2-(4-fluoro-2-methylphenoxy)-5-((12-methylphenyl)carbonylamino)pyridine	336		2-(2-methylphenoxy)-5-((12-methylphenyl)carbonylamino)pyridine	318	
2-(4-fluoro-2-methylphenoxy)-5-((12-trifluoromethylphenyl)carbonylamino)pyridine	390		2-(2,4-dimethylphenoxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	387	
2-(4-fluoro-2-methylphenoxy)-5-((12-fluorophenyl)carbonylamino)pyridine	340		2-(2,4-dimethylphenoxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	346	
2-(2-isopropylphenoxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	401		2-(2,4-dimethylphenoxy)-5-((12-chlorophenyl)carbonylamino)pyridine	353	
2-(2-isopropylphenoxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	360		2-(2,4-dimethylphenoxy)-5-((12-methylphenyl)carbonylamino)pyridine	332	
2-(2-isopropylphenoxy)-5-((12-methylphenyl)carbonylamino)pyridine	346		2-(4-chlorophenoxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	394	
2-(1-naphthylloxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	409		2-(4-chlorophenoxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	353	
2-(1-naphthylloxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	368		2-(2-methylcyclohexylamino)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	378	
2-(1-naphthylloxy)-5-((12-methylphenyl)carbonylamino)pyridine	354		2-(2-methylcyclohexylamino)-5-((12-methylphenyl)carbonylamino)pyridine	323	
2-(cyclohexylloxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	365		2-(cyclohexylamino)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	364	
2-(cyclohexylloxy)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	324		2-(cyclohexylamino)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	323	
2-(cyclohexylloxy)-5-((12-chlorophenyl)carbonylamino)pyridine	331		2-(cyclohexylamino)-5-((12-methylphenyl)carbonylamino)pyridine	309	
2-(cyclohexylloxy)-5-((12-methylphenyl)carbonylamino)pyridine	310		2-(2-methylamino)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	372	
2-(2-methylphenoxy)-5-((12,6-dichlorophenyl)carbonylamino)pyridine	373		2-(2-methylamino)-5-((12,6-dimethylphenyl)carbonylamino)pyridine	331	

2-(2-methylanilino)-5-((2-methylphenyl)carbonylamino)pyridine 317

2-(4-chloro-2-methylanilino)-5-((2,6-dichlorophenyl)carbonylamino)pyridine 407

2-(4-chloro-2-methylanilino)-5-((2,6-dimethylphenyl)carbonylamino)pyridine 366

2-(4-chloro-2-methylanilino)-5-((2-methylphenyl)carbonylamino)pyridine 352

2-(2,4-dimethylanilino)-5-((2,6-dichlorophenyl)carbonylamino)pyridine 386

2-(2,4-dimethylanilino)-5-((2,6-dimethylphenyl)carbonylamino)pyridine 345

2-(2,4-dimethylanilino)-5-((2-methylphenyl)carbonylamino)pyridine 331

2-(2,4-dimethylanilino)-5-((2-chlorophenyl)carbonylamino)pyridine 352

2-(2,4-dimethylanilino)-5-((2-fluorophenyl)carbonylamino)pyridine 335

2-(4-chloro-2-methyl-thiophenyl)-5-((2,6-dichlorophenyl)carbonylamino)pyridine 424

2-(4-chloro-2-methyl-thiophenyl)-5-((2,6-dimethylphenyl)carbonylamino)pyridine 383

2-(4-chloro-2-methyl-thiophenyl)-5-((2-methylphenyl)carbonylamino)pyridine 369

Example 7

The compounds listed in Table 4 were prepared from substituted 5-aminopyridine compounds and the appropriate acid chloride in the same manner as N-(2-(4-chloro-2-methyl-phenoxy)-pyridin-5-yl)-benzamide was prepared.

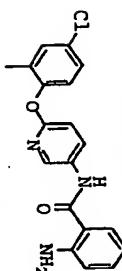
Table 4

	MS (m/z)
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dichlorophenyl)carbonylamino)-3-methyl-pyridine	422
2-(4-Chloro-2-methyl-phenoxy)-5-((2-chlorophenyl)carbonylamino)-3-methyl-pyridine	387
2-(4-Chloro-2-methyl-phenoxy)-5-((2-methylphenyl)carbonylamino)-3-methyl-pyridine	367
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dimethylphenyl)carbonylamino)-3-methyl-pyridine	332
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dichlorophenyl)carbonylamino)-4-methyl-pyridine	422
2-(4-Chloro-2-methyl-phenoxy)-5-((2-fluoro-6-trifluoromethylphenyl)carbonylamino)-4-methyl-pyridine	439
2-(4-Chloro-2-methyl-phenoxy)-5-((2,4,6-triisopropylphenyl)carbonylamino)-4-methyl-pyridine	479
2-(4-Chloro-2-methyl-phenoxy)-5-((2-methylphenyl)carbonylamino)-6-methyl-pyridine	367
2-(4-Chloro-2-methyl-phenoxy)-5-((2-chlorophenyl)carbonylamino)-6-methyl-pyridine	387
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dichlorophenyl)carbonylamino)-6-methyl-pyridine	422
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dichlorophenyl)carbonylamino)-6-amino-pyridine	423
2-(4-Chloro-2-methyl-phenoxy)-5-((2-chlorophenyl)carbonylamino)-6-amino-pyridine	388
2-(4-Chloro-2-methyl-phenoxy)-5-((2,6-dimethylphenyl)carbonylamino)-6-amino-pyridine	382

2-(4-chloro-2-methyl-phenoxy)-5-((2-methylphenyl)carbonylamino)-6-amino-pyridine

368

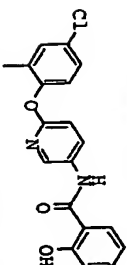
Example 8



5 Preparation of 2-amino-N-(5-(4-chloro-2-methyl-phenoxy)-pyridin-3-yl)-benzamide

N-(6-(4-chloro-2-methyl-phenoxy)-pyridin-3-yl)-2-nitro-benzamide (301 mg, 0.7 mmol) was dissolved in 95% ethanol (4 mL) and treated with 20% palladium hydroxide on carbon (Pearlman's catalyst, 50 mg) and subjected to a hydrogen atmosphere (40 psi) for 2 hours. The catalyst was removed by filtration and the solvents were removed in vacuo. The product was purified by hexanes chromatography on SiO₂ using 1:1 ethyl acetate / hexanes as eluent. MS (m/z): 353/355 (M+H)⁺; C₁₈H₁₆N₃O₂Cl requires 353.8.

Example 9



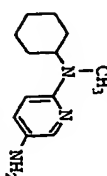
20 Preparation of N-(5-(4-chloro-2-methyl-phenoxy)-pyridin-3-yl)-2-hydroxy-benzamide

Acetic acid 2-(6-(4-chloro-2-methyl-phenoxy)-pyridin-3-ylcarbonyl)-phenyl ester (304 mg, 0.77 mmol) dissolved in tetrahydrofuran (3.8 mL) was treated with an aqueous lithium hydroxide solution (1.0 M, 3.8 mL, 3.8 mmol).

The solution was stirred for 30 minutes at 22°C then quenched with aqueous saturated NH₄Cl. The mixture was diluted with ethyl acetate then the organics were washed

with water, 2x saturated NaHCO₃, saturated NaCl, dried over Na₂SO₄, and concentrated in vacuo. MS (m/z): 354/356 (M+H)⁺; C₁₈H₁₆N₃O₂Cl requires 354.8.

Example 10



Preparation of 2-(N-cyclohexyl-N-methylamino)-5-amino-pyridine

Step A: 2-(cyclohexylamino)-5-nitro-pyridine Sodium hydride (60% dispersion in mineral oil, 1.99 g, 49.8 mmol) was washed 3x with hexanes then a solution of cyclohexylamine (3.8 mL, 33.2 mmol) dissolved in tetrahydrofuran (50 mL) was added. After stirring for 30 minutes at 22 °C, 2-chloro-5-nitropyridine (5.00 g, 31.5 mmol) was added and the reaction mixture was heated to reflux for 3 hours. The solution was cooled to ambient temperature, quenched with saturated aqueous NH₄Cl and concentrated in vacuo. The residue was redissolved in ethyl acetate then washed 2x with saturated NaHCO₃, saturated NaCl, dried over anhydrous Na₂SO₄, and concentrated in vacuo. The product was recovered as a brown oil.

Step B: 2-(N-cyclohexyl-N-methylamino)-5-nitro-pyridine Sodium hydride (60% dispersion in mineral oil, 0.38 g, 9.48 mmol) was washed 3x with hexanes then a solution of 2-cyclohexylamino-5-nitropyridine (1.88 g, 8.5 mmol) dissolved in dimethylformamide (20 mL) was added. After stirring for 30 minutes at 22°C, the reaction mixture was cooled to 0°C and methyl iodide (0.55 mL, 8.9 mmol) was added. The solution was stirred for 1.5 hours at 0°C followed by quenching with saturated aqueous NH₄Cl. The reaction mixture was diluted with ethyl acetate and

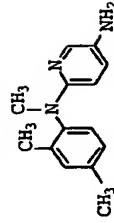
extracted 5x with water (200 mL), saturated NaCl, dried over Na₂SO₄ and concentrated in vacuo oil was chromatographed on SiO₂ using 2:1 hexanes / ethyl acetate as eluent.

5

Step C: 2-(N-Cyclohexyl-N-methylamino)-5-amino-pyridine
Cyclohexyl-methyl-(5-nitro-pyridin-2-yl)-amine (1.72 g, 7.3 mmol) was dissolved in ethanol (80 mL) and treated with 20% palladium hydroxide on carbon (Pearlman's catalyst, 0.5 g) and the mixture was shaken under a hydrogen atmosphere (50 psi) for 6 hours. The catalyst was removed by filtration through celite then the filtrate was concentrated in vacuo and the resultant oil was chromatographed on SiO₂ using 1:1 ethyl acetate / hexanes as eluent. MS (m/z): 206 (M+H)⁺; C₁₁H₁₆N₂, requires 205.3.

15

Example 11

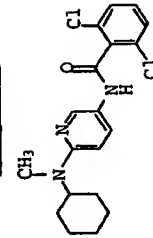


20 Preparation of 2-(N-(2,4-dimethylphenyl)-N-methylamino)-5-amino-pyridine

2-(N-(2,4-dimethylphenyl)-N-methylamino)-5-amino-pyridine was prepared from 1-amino-2,4-dimethylbenzene and 2-chloro-5-nitropyridine in the same manner as 2-(N-Cyclohexyl-N-methylamino)-5-amino-pyridine was prepared.

25

Example 12



Preparation of 2-(N-(2,6-dichlorophenyl)-N-methylamino)-5-amino-pyridine

30

2-(N-Cyclohexyl-N-methylamino)-5-amino-pyridine (26 mg, 0.13 mmol) dissolved in methylene chloride (0.25 mL) was treated with triethylamine (0.026 mL, 0.18 mmol)

followed by a solution of 2,6-dichlorobenzoyl chloride

5 (31 mg, 0.15 mmol) dissolved in methylene chloride (0.15 mL). The reaction mixture was shaken at 22°C for 18

hours followed by quenching with saturated aqueous NH₄Cl and stirring for an additional 5 hours. The organic layer was separated and dried over Na₂SO₄, then

10 concentrated in vacuo. The crude product was purified by chromatography on SiO₂ using 1:1 ethyl acetate /

hexane as eluent. MS (m/z): 378/380 (M+H)⁺; C₁₇H₁₈N₂OCl₂ requires 377.

15

Example 13

The compounds listed in Table 5 were prepared from substituted 5-aminopyridine compounds and the appropriate acid chloride in the same manner as 2,6-Dichloro-N-(2-(N'-cyclohexyl-N'-methylamino)-pyridin-5-yl)-benzamide was prepared.

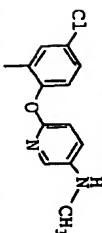
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Table 5

	MS (m/z)
2-(N-cyclohexyl-N-methylamino)-5-((2,6-dichlorophenyl)carbonylamino)pyridine	378
2-(N-cyclohexyl-N-methylamino)-5-((2-chlorophenyl)carbonylamino)pyridine	344
2-(N-cyclohexyl-N-methylamino)-5-((2-methylphenyl)carbonylamino)pyridine	323
2-(N-cyclohexyl-N-methylamino)-5-((2,6-dimethylphenyl)carbonylamino)pyridine	337
2-(2,4-dimethylphenyl)-5-((2,6-dimethylphenyl)carbonylamino)pyridine	359

2-(2,4-dimethylphenyl)-5-(2-methylphenyl)carbonylamino pyridine	345
2-(2,4-dimethylphenyl)-5-(2-chlorophenyl)carbonylamino pyridine	366
2-(2,4-dimethylphenyl)-5-(2-fluorophenyl)carbonylamino pyridine	349
2-(2,4-dimethylphenyl)-5-(2,6-dichlorophenyl)carbonylamino pyridine	400

Example 14



5 Preparation of 2-(4-chloro-2-methyl-phenoxyl)-5-(N-methylamino)pyridine

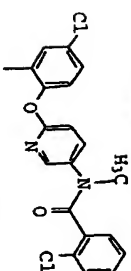
2-(4-chloro-2-methyl-phenoxyl)-5-amino pyridine (2.15 g, 9.16 mmol) was combined with powdered sodium hydroxide (1.46 g, 36.6 mmol), potassium carbonate (1.27 g, 9.16 mmol), tetrabutyl ammonium bromide (60 mg, 0.18 mmol) and toluene (10 mL) was stirred for 1 hour at 35°C. A solution of dimethyl sulfate (0.91 mL, 9.6 mmol) dissolved in toluene (5 mL) was added slowly. The mixture was heated at 35°C for 20 hours. After cooling, the solids were removed by filtration and the solvent was concentrated in vacuo. The desired material was purified by chromatography on SiO₂, using 30% ethyl acetate / hexanes as eluent. MS (m/z): 248/250 (M+H)⁺; C₁₄H₁₄NOCl requires 249.

5 Preparation of 2,6-dichloro-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide

2-(4-chloro-2-methyl-phenoxyl)-5-(N-methylamino)pyridine (32 mg, 0.13 mmol) dissolved in methylene chloride (0.25 mL) was treated with triethylamine (0.026 mL, 0.18 mmol) followed by a solution of 2,6-dichlorobenzoyl chloride (0.15 mL, 0.15 mmol) dissolved in methylene chloride (0.15 mL). The reaction mixture was shaken at 22°C for 18 hours followed by quenching with saturated aqueous NH₄Cl and stirring for an additional 5 hours. The organic layer was separated and dried over Na₂SO₄, then concentrated in vacuo. The crude product was purified by chromatography on SiO₂, using 1:1 ethyl acetate / hexane as eluent. MS (m/z): 422/424 (M+H)⁺; C₂₀H₁₆N₂O₂Cl₃ requires 422.

20

Example 15



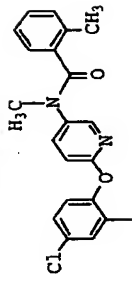
25 Preparation of 2-chloro-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide

2-chloro-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide was prepared from 2-(4-chloro-2-methyl-phenoxyl)-5-(N-methylamino)pyridine and 2-chlorobenzoyl chloride in the same manner as 2,6-dichloro-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide was prepared.

30

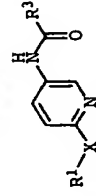
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Example 17

Preparation of 2-Methyl-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide

- 5 2-Methyl-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide was prepared from 2-(4-Chloro-2-methyl-phenoxyl)-5-(N-methylamino)pyridine and 2-methylbenzoyl chloride in the same manner as 2,6-Dichloro-N-(6-(4-chloro-2-methyl-phenoxyl)-pyridin-3-yl)-N-methyl-benzamide was prepared.
- 10

Example 18

General procedure for the synthesis of 2-substituted-5-acylamino-pyridines

- 15 A solution of the 2-substituted-5-aminopyridine (10 mmol), triethylamine (20 mmol) and an acid chloride (20 mmol) in ethanol free chloroform (250 mL) was shaken for 16 hours. The mixture was then diluted with saturated aqueous sodium hydrogencarbonate (50 mL) and dichloromethane (500 mL), and shaken for 30 min. The mixture was then filtered through anhydrous magnesium sulfate, washing with dichloromethane (250 mL). Concentration of the filtrate under reduced pressure afforded the desired 2-substituted-5-acylamino-pyridines.
- 20
- 25

The compounds listed in Table 6 were prepared from substituted 5-aminopyridine compounds and the appropriate acid chloride according to the general procedure above.

30

58

Table 6

R ¹ X	R ¹	MS (m/z)
4-chloro-2-methylphenoxyl	4-biphenyl	415
4-chloro-2-methylphenoxyl	3,4-dimethoxyphenyl	319
4-chloro-2-methylphenoxyl	2-(trifluoromethyl)phenyl	407
4-chloro-2-methylphenoxyl	2,4-difluorophenyl	375
4-chloro-2-methylphenoxyl	4-cyanophenyl	364
4-chloro-2-methylphenoxyl	3-(trifluoromethyl)phenyl	407
4-chloro-2-methylphenoxyl	3-cyanophenyl	364
4-chloro-2-methylphenoxyl	2-naphthyl	389
4-chloro-2-methylphenoxyl	2-methoxyphenyl	369
4-chloro-2-methylphenoxyl	3,4,5-trimethylphenyl	429
4-chloro-2-methylphenoxyl	4-nitrophenyl	384
4-chloro-2-methylphenoxyl	3,4-dichlorophenyl	408
4-chloro-2-methylphenoxyl	5-nitrofuran-2-yl	374
4-chloro-2-methylphenoxyl	3-bromophenyl	418

4-chloro-2-methylphenoxy	3-pyridyl	340
4-chloro-2-methylphenoxy	2-ethoxynaphth-1-yl	433
4-chloro-2-methylphenoxy	2,3-dichlorophenyl	408
4-chloro-2-methylphenoxy	3-nitrophenyl	384
4-chloro-2-methylphenoxy	6-chloropyrid-3-yl	374
4-chloro-2-methylphenoxy	4-(trifluoromethoxy)phenyl	423
4-chloro-2-methylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	425
4-chloro-2-methylphenoxy	2-acetoxypheyl	397
4-chloro-2-methylphenoxy	5-methylisoxazol-3-yl	344
4-chloro-2-methylphenoxy	2-(phenylthio)pyrid-3-yl	448
4-chloro-2-methylphenoxy	2-(trifluoromethoxy)phenyl	423
4-chloro-2-methylphenoxy	1-phenyl-5-propyl-pyrazin-4-yl	447
4-chloro-2-methylphenoxy	2-ethoxyphenyl	383
4-chloro-2-methylphenoxy	3-chlorothi-2-yl	379
4-chloro-2-methylphenoxy	3-bromothi-2-yl	424

4-chloro-2-methylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	399
4-chloro-2-methylphenoxy	3,5-dichlorophenyl	408
4-chloro-2-methylphenoxy	2-(propylthio)pyridin-3-yl	414
4-chloro-2-methylphenoxy	2-(ethylthio)pyridin-3-yl	400
4-chloro-2-methylphenoxy	3-bromopyridin-5-yl	419
4-chloro-2-methylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	361
4-chloro-2-methylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	399
4-chloro-2-methylphenoxy	3-chlorobenzo[b]thiophen-2-yl	429
4-chloro-2-methylphenoxy	4-chlorophenyl	373
4-chloro-2-methylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	420
4-chloro-2-methylphenoxy	benzo[b]thiophen-2-yl	395
4-chloro-2-methylphenoxy	3,4-dimethylphenyl	367
4-chloro-2-methylphenoxy	2-(phenoxyl)pyridin-3-yl	432
4-chloro-2-methylphenoxy	2-(methylthio)pyridin-3-yl	386
4-chloro-2-methylphenoxy	5-methyl-3-phenylisoxazol-4-yl	420

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4-chloro-2-methylphenoxy	2-bromophenyl	418
4-chloro-2-methylphenoxy	4-bromophenyl	418
4-chloro-2-methylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	425
4-chloro-2-methylphenoxy	3-(trifluoromethoxy)phenyl	423
4-chloro-2-methylphenoxy	9-fluorenon-4-yl	441
4-chloro-2-methylphenoxy	isoxazol-5-yl	330
4-chloro-2-methylphenoxy	benzofuroxan-5-yl	397
4-chloro-2-methylphenoxy	2-chloropyrid-3-yl	374
4-chloro-2-methylphenoxy	3,5-difluorophenyl	375
4-chloro-2-methylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	446
4-chloro-2-methylphenoxy	pyridin-4-yl	340
4-chloro-2-methylphenoxy	anthraquinon-2-yl	469
4-chloro-2-methylphenoxy	2-iodophenyl	465
1-naphthoxy	4-biphenyl	416
1-naphthoxy	3,4-dimethoxyphenyl	400
1-naphthoxy	2-(trifluoromethyl)phenyl	408
1-naphthoxy	2,4-difluorophenyl	376
1-naphthoxy	4-cyanophenyl	365

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1-naphthoxy	3-(trifluoromethyl)phenyl	408
1-naphthoxy	3-cyanophenyl	365
1-naphthoxy	2-naphthyl	390
1-naphthoxy	2-methoxyphenyl	370
1-naphthoxy	3,4,5-trimethylphenyl	430
1-naphthoxy	4-nitrophenyl	385
1-naphthoxy	3,4-dichlorophenyl	409
1-naphthoxy	5-nitrofuran-2-yl	375
1-naphthoxy	3-bromophenyl	419
1-naphthoxy	3-pyridyl	341
1-naphthoxy	2-ethoxynaphth-1-yl	334
1-naphthoxy	2,3-dichlorophenyl	409
1-naphthoxy	3-nitrophenyl	385
1-naphthoxy	6-chloropyrid-3-yl	376
1-naphthoxy	4-(trifluoromethoxy)phenyl	424
1-naphthoxy	2-fluoro-4-(trifluoromethyl)phenyl	426
1-naphthoxy	3-bromochlorophenyl	425
1-naphthoxy	2-acetoxyphenyl	398
1-naphthoxy	5-methylisoxazol-3-yl	345
1-naphthoxy	2-(phenylthio)pyrid-3-yl	449
1-naphthoxy	2-(trifluoromethoxy)phenyl	424
1-naphthoxy	1-phenyl-5-propylpyrazin-4-yl	448
1-naphthoxy	2-ethoxyphenyl	384
1-naphthoxy	3-chlorothiien-2-yl	381
1-naphthoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	400

1-naphthoxy	3,5-dichlorophenyl	409	1-naphthoxy	2,6-difluorophenyl	376
1-naphthoxy	2-(propylthio)pyridin-3-yl	415	1-naphthoxy	2-chlorophenyl	375
1-naphthoxy	2-(ethylthio)pyridin-3-yl	401	1-naphthoxy	3-(chloromethyl)phenyl	389
1-naphthoxy	3-bromopyridin-5-yl	420	1-naphthoxy	4-(2-(2-methyl)propyl)phenyl	396
1-naphthoxy	4-methyl-1,2,3-thiadiazol-5-yl	362	1-naphthoxy	3-chlorophenyl	375
1-naphthoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	400	1-naphthoxy	2-nitrophenyl	385
1-naphthoxy	3-chlorobenzo[b]thiophen-2-yl	431	1-naphthoxy	3,5-dimethoxyphenyl	400
1-naphthoxy	4-chlorophenyl	375	1-naphthoxy	2,6-dichlorophenyl	409
1-naphthoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	421	1-naphthoxy	2,4-dichlorophenyl	409
1-naphthoxy	benzo[b]thiophen-2-yl	396	1-naphthoxy	4-fluorophenyl	358
1-naphthoxy	3,4-dimethylphenyl	368	1-naphthoxy	4-butylphenyl	396
1-naphthoxy	2-(phenoxy)pyridin-3-yl	433	1-naphthoxy	2-methylphenyl	354
1-naphthoxy	2-(methylthio)pyridin-3-yl	387	1-naphthoxy	4-ethylphenyl	340
1-naphthoxy	5-methyl-3-phenylisoxazol-4-yl	421	1-naphthoxy	2,3-difluorophenyl	368
1-naphthoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	444	1-naphthoxy	2,6-dimethoxyphenyl	376
1-naphthoxy	2-chloro-6-methylpyridin-4-yl	390	1-naphthoxy	2,6-dimethoxyphenyl	400
1-naphthoxy	3,5-dimethylisoxazol-4-yl	359	1-naphthoxy	3,4-difluorophenyl	376
1-naphthoxy	1-naphthyl	390	1-naphthoxy	2,5-difluorophenyl	376
1-naphthoxy	2-fluorophenyl	358	1-naphthoxy	4-ethoxyphenyl	384
1-naphthoxy	4-propylphenyl	382	1-naphthoxy	2,4,6-trichlorophenyl	444
1-naphthoxy	4-(trifluoromethyl)phenyl	408	1-naphthoxy	3-methylphenyl	354
1-naphthoxy	3-fluorophenyl	358	1-naphthoxy	2-fluoro-5-(trifluoromethyl)phenyl	426
			1-naphthoxy	3-methoxyphenyl	370
			1-naphthoxy	thien-2-yl	346
			1-naphthoxy	2-bromophenyl	419
			1-naphthoxy	4-bromophenyl	419

1-naphthoxy	4-fluoro-3-(trifluoromethyl)phenyl	426
1-naphthoxy	3-(trifluoromethoxy)phenyl	424
1-naphthoxy	9-fluorenon-4-yl	442
1-naphthoxy	isoxazol-5-yl	331
1-naphthoxy	benzofuroxan-5-yl	398
1-naphthoxy	2-chloropyrid-3-yl	376
1-naphthoxy	3,5-difluorophenyl	376
1-naphthoxy	2-(4-methylphenoxy)pyridin-3-yl	447
1-naphthoxy	pyridin-4-yl	341
1-naphthoxy	anthraquinon-2-yl	470
1-naphthoxy	2-iodophenyl	466
2-(2-propyl)phenoxy	4-biphenyl	408
2-(2-propyl)phenoxy	3,4-dimethoxyphenyl	392
2-(2-propyl)phenoxy	2-(trifluoromethyl)phenyl	400
2-(2-propyl)phenoxy	2,4-difluorophenyl	368
2-(2-propyl)phenoxy	4-cyanophenyl	357
2-(2-propyl)phenoxy	3-(trifluoromethyl)phenyl	400
2-(2-propyl)phenoxy	3-cyanophenyl	357
2-(2-propyl)phenoxy	2-naphthyl	382
2-(2-propyl)phenoxy	2-methoxyphenyl	362
2-(2-propyl)phenoxy	3,4,5-trimethylphenyl	422
2-(2-propyl)phenoxy	4-nitrophenyl	377
2-(2-propyl)phenoxy	3,4-dichlorophenyl	401
2-(2-propyl)phenoxy	5-nitrofuran-2-yl	367
2-(2-propyl)phenoxy	3-bromophenyl	411
2-(2-propyl)phenoxy	3-pyridyl	333

2-(2-propyl)phenoxy	2-ethoxynaphth-1-yl	426
2-(2-propyl)phenoxy	2,3-dichlorophenyl	401
2-(2-propyl)phenoxy	3-nitrophenyl	377
2-(2-propyl)phenoxy	6-chloropyrid-3-yl	368
2-(2-propyl)phenoxy	4-(trifluoromethoxy)phenyl	416
2-(2-propyl)phenoxy	2-fluoro-4-(trifluoromethyl)phenyl	418
2-(2-propyl)phenoxy	3-bromothiophenyl	417
2-(2-propyl)phenoxy	2-acetoxypheyl	390
2-(2-propyl)phenoxy	5-methylisoxazol-3-yl	337
2-(2-propyl)phenoxy	2-(phenylthio)pyrid-3-yl	442
2-(2-propyl)phenoxy	2-(trifluoromethoxy)phenyl	416
2-(2-propyl)phenoxy	1-phenyl-5-propylpyrazin-4-yl	441
2-(2-propyl)phenoxy	2-ethoxyphenyl	376
2-(2-propyl)phenoxy	3-chlorochien-2-yl	373
2-(2-propyl)phenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	392
2-(2-propyl)phenoxy	3,5-dichlorophenyl	401
2-(2-propyl)phenoxy	2-(propylthio)pyridin-3-yl	407
2-(2-propyl)phenoxy	2-(ethylthio)pyridin-3-yl	393
2-(2-propyl)phenoxy	3-bromopyridin-5-yl	412
2-(2-propyl)phenoxy	4-methyl-1,2,3-thiadiazol-5-yl	354
2-(2-propyl)phenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	392
2-(2-propyl)phenoxy	3-chlorobenzo[b]thiophen-2-yl	423
2-(2-propyl)phenoxy	4-chlorophenyl	367

2-(2-propyl)phenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	413
2-(2-propyl)phenoxy	benzo(b)thiophen-2-yl	388
2-(2-propyl)phenoxy	3,4-dimethylphenyl	360
2-(2-propyl)phenoxy	2-(phenoxy)pyridin-3-yl	425
2-(2-propyl)phenoxy	2-(methylthio)pyridin-3-yl	379
2-(2-propyl)phenoxy	5-methyl-3-phenylisoxazol-4-yl	413
2-(2-propyl)phenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	436
2-(2-propyl)phenoxy	2-chloro-6-methylpyridin-4-yl	382
2-(2-propyl)phenoxy	3,5-dimethylisoxazol-4-yl	351
2-(2-propyl)phenoxy	1-naphthyl	382
2-(2-propyl)phenoxy	2-fluorophenyl	350
2-(2-propyl)phenoxy	4-propylphenyl	374
2-(2-propyl)phenoxy	4-(trifluoromethyl)phenyl	400
2-(2-propyl)phenoxy	3-fluorophenyl	350
2-(2-propyl)phenoxy	2,6-difluorophenyl	368
2-(2-propyl)phenoxy	2-chlorophenyl	367
2-(2-propyl)phenoxy	3-(chloromethyl)phenyl	381
2-(2-propyl)phenoxy	4-(2-(2-methyl)propyl)phenyl	388
2-(2-propyl)phenoxy	3-chlorophenyl	367
2-(2-propyl)phenoxy	2-nitrophenyl	377
2-(2-propyl)phenoxy	3,5-dimethoxyphenyl	392
2-(2-propyl)phenoxy	2,6-dichlorophenyl	401
2-(2-propyl)phenoxy	2,4-dichlorophenyl	401

2-(2-propyl)phenoxy	4-fluorophenyl	
2-(2-propyl)phenoxy	4-butylphenyl	
2-(2-propyl)phenoxy	2-methylphenyl	
2-(2-propyl)phenoxy	phenyl	
2-(2-propyl)phenoxy	4-ethylphenyl	
2-(2-propyl)phenoxy	2,3-difluorophenyl	
2-(2-propyl)phenoxy	2,6-dimethoxyphenyl	392
2-(2-propyl)phenoxy	3,4-difluorophenyl	368
2-(2-propyl)phenoxy	2,5-difluorophenyl	368
2-(2-propyl)phenoxy	4-ethoxyphenyl	376
2-(2-propyl)phenoxy	2,4,6-trichlorophenyl	436
2-(2-propyl)phenoxy	3-methylphenyl	346
2-(2-propyl)phenoxy	2-fluoro-5-(trifluoromethyl)phenyl	418
2-(2-propyl)phenoxy	3-methoxyphenyl	362
2-(2-propyl)phenoxy	thien-2-yl	338
2-(2-propyl)phenoxy	2-bromophenyl	411
2-(2-propyl)phenoxy	4-bromophenyl	411
2-(2-propyl)phenoxy	4-fluoro-3-(trifluoromethyl)phenyl	418
2-(2-propyl)phenoxy	3-(trifluoromethoxy)phenyl	416
2-(2-propyl)phenoxy	9-fluorenon-4-yl	434
2-(2-propyl)phenoxy	isoxazol-5-yl	323
2-(2-propyl)phenoxy	benzofuroxan-5-yl	390
2-(2-propyl)phenoxy	2-chloropyridin-3-yl	368
2-(2-propyl)phenoxy	3,5-difluorophenyl	368
2-(2-propyl)phenoxy	2-(4-methylphenoxy)pyridin-3-yl	439

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2-(2-propyl)phenoxy	pyridin-4-yl	333
2-(2-propyl)phenoxy	anthraquinon-2-yl	462
2-(2-propyl)phenoxy	2-iodophenyl	458
3-fluoro-5-methylphenoxy	4-biphenyl	398
3-fluoro-5-methylphenoxy	3,4-dimethoxyphenyl	382
3-fluoro-5-methylphenoxy	2-(trifluoromethyl)phenyl	390
3-fluoro-5-methylphenoxy	2,4-difluorophenyl	358
3-fluoro-5-methylphenoxy	4-cyanophenyl	347
3-fluoro-5-methylphenoxy	3-(trifluoromethyl)phenyl	390
3-fluoro-5-methylphenoxy	3-cyanophenyl	347
3-fluoro-5-methylphenoxy	2-naphthyl	372
3-fluoro-5-methylphenoxy	2-methoxyphenyl	352
3-fluoro-5-methylphenoxy	3,4,5-trimethylphenyl	412
3-fluoro-5-methylphenoxy	4-nitrophenyl	367
3-fluoro-5-methylphenoxy	3,4-dichlorophenyl	391
3-fluoro-5-methylphenoxy	5-nitrofuran-2-yl	357
3-fluoro-5-methylphenoxy	3-bromophenyl	401

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3-fluoro-5-methylphenoxy	3-pyridyl	323
3-fluoro-5-methylphenoxy	2-ethoxynaphth-1-yl	416
3-fluoro-5-methylphenoxy	2,3-dichlorophenyl	391
3-fluoro-5-methylphenoxy	3-nitrophenyl	367
3-fluoro-5-methylphenoxy	6-chloropyrid-3-yl	358
3-fluoro-5-methylphenoxy	4-(trifluoromethoxy)phenyl	406
3-fluoro-5-methylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	408
3-fluoro-5-methylphenoxy	3-bromobenzyl	407
3-fluoro-5-methylphenoxy	2-acetoxypheyl	380
3-fluoro-5-methylphenoxy	5-methylisoxazol-3-yl	327
3-fluoro-5-methylphenoxy	2-(phenylthio)pyrid-3-yl	431
3-fluoro-5-methylphenoxy	2-(trifluoromethoxy)phenyl	406
3-fluoro-5-methylphenoxy	1-phenyl-5-propylpyrazin-4-yl	430
3-fluoro-5-methylphenoxy	2-ethoxyphenyl	366
3-fluoro-5-methylphenoxy	3-chlorothien-2-yl	363
3-fluoro-5-methylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	382

3-fluoro-5-methylphenoxy	3,5-dichlorophenyl	391	3-fluoro-5-methylphenoxy	2-chloro-6-methylpyridin-4-yl	372
3-fluoro-5-methylphenoxy	2-(propylthio)pyridin-3-yl	397	3-fluoro-5-methylphenoxy	3,5-dimethylisoxazol-4-yl	341
3-fluoro-5-methylphenoxy	2-(ethylthio)pyridin-3-yl	383	3-fluoro-5-methylphenoxy	1-naphthyl	372
3-fluoro-5-methylphenoxy	3-bromopyridin-5-yl	402	3-fluoro-5-methylphenoxy	2-fluorophenyl	340
3-fluoro-5-methylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	344	3-fluoro-5-methylphenoxy	4-propylphenyl	364
3-fluoro-5-methylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	382	3-fluoro-5-methylphenoxy	4-(trifluoromethyl)phenyl	390
3-fluoro-5-methylphenoxy	3-chlorobenzo[b]thiophen-2-yl	413	3-fluoro-5-methylphenoxy	3-fluorophenyl	340
3-fluoro-5-methylphenoxy	4-chlorophenyl	357	3-fluoro-5-methylphenoxy	2,6-difluorophenyl	358
3-fluoro-5-methylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	403	3-fluoro-5-methylphenoxy	2-chlorophenyl	357
3-fluoro-5-methylphenoxy	benzo[b]thiophen-2-yl	378	3-fluoro-5-methylphenoxy	3-(chloromethyl)phenyl	371
3-fluoro-5-methylphenoxy	3,4-dimethylphenyl	350	3-fluoro-5-methylphenoxy	4-(2-(2-methyl)propyl)phenyl	378
3-fluoro-5-methylphenoxy	2-(phenoxy)pyridin-3-yl	415	3-fluoro-5-methylphenoxy	3-chlorophenyl	357
3-fluoro-5-methylphenoxy	2-(methylthio)pyridin-3-yl	369	3-fluoro-5-methylphenoxy	2-nitrophenyl	367
3-fluoro-5-methylphenoxy	5-methyl-3-phenylisoxazol-4-yl	403	3-fluoro-5-methylphenoxy	3,5-dimethoxyphenyl	382
3-fluoro-5-methylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	426	3-fluoro-5-methylphenoxy	2,6-dichlorophenyl	391

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3-fluoro-5-methylphenoxy	2,4-dichlorophenyl	391
3-fluoro-5-methylphenoxy	4-fluorophenyl	340
3-fluoro-5-methylphenoxy	4-butylphenyl	378
3-fluoro-5-methylphenoxy	2-methylphenyl	336
3-fluoro-5-methylphenoxy	phenyl	322
3-fluoro-5-methylphenoxy	4-ethylphenyl	350
3-fluoro-5-methylphenoxy	2,3-difluorophenyl	358
3-fluoro-5-methylphenoxy	2,6-dimethoxyphenyl	382
3-fluoro-5-methylphenoxy	3,4-difluorophenyl	358
3-fluoro-5-methylphenoxy	2,5-difluorophenyl	358
3-fluoro-5-methylphenoxy	4-ethoxyphenyl	366
3-fluoro-5-methylphenoxy	2,4,6-trichlorophenyl	426
3-fluoro-5-methylphenoxy	3-methylphenyl	336
3-fluoro-5-methylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	408
3-fluoro-5-methylphenoxy	3-methoxyphenyl	352

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3-fluoro-5-methylphenoxy	thien-2-yl	328
3-fluoro-5-methylphenoxy	2-bromophenyl	401
3-fluoro-5-methylphenoxy	4-bromophenyl	401
3-fluoro-5-methylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	408
3-fluoro-5-methylphenoxy	3-(trifluoromethoxy)phenyl	406
3-fluoro-5-methylphenoxy	9-fluorenon-4-yl	424
3-fluoro-5-methylphenoxy	isoxazol-5-yl	313
3-fluoro-5-methylphenoxy	benzofuroxan-5-yl	380
3-fluoro-5-methylphenoxy	2-chloropyrid-3-yl	358
3-fluoro-5-methylphenoxy	3,5-difluorophenyl	358
3-fluoro-5-methylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	429
3-fluoro-5-methylphenoxy	pyridin-4-yl	323
3-fluoro-5-methylphenoxy	anthraquinon-2-yl	452
3-fluoro-5-methylphenoxy	2-iodophenyl	448
2-methylpyrid-3-yl	4-biphenyl	381
2-methylpyrid-3-yl	3,4-dimethoxyphenyl	365

2-methylpyrid-3-yloxy 2-(trifluoromethyl)phenyl	373
2-methylpyrid-3-yloxy 2,4-difluorophenyl	341
2-methylpyrid-3-yloxy 4-cyanophenyl	330
2-methylpyrid-3-yloxy 3-(trifluoromethyl)phenyl	373
2-methylpyrid-3-yloxy 3-cyanophenyl	330
2-methylpyrid-3-yloxy 2-naphthyl	355
2-methylpyrid-3-yloxy 2-methoxyphenyl	335
2-methylpyrid-3-yloxy 3,4,5-trimethylphenyl	395
2-methylpyrid-3-yloxy 4-nitrophenyl	350
2-methylpyrid-3-yloxy 3,4-dichlorophenyl	374
2-methylpyrid-3-yloxy 5-nitrofur-2-yl	340
2-methylpyrid-3-yloxy 3-bromophenyl	384
2-methylpyrid-3-yloxy 3-pyridyl	306
2-methylpyrid-3-yloxy 2-ethoxynaphth-1-yl	399
2-methylpyrid-3-yloxy 2,3-dichlorophenyl	374
2-methylpyrid-3-yloxy 3-nitrophenyl	350
2-methylpyrid-3-yloxy 6-chloropyrid-3-yl	341
2-methylpyrid-3-yloxy 4-(trifluoromethoxy)phenyl	389
2-methylpyrid-3-yloxy 2-fluoro-4-(trifluoromethyl)phenyl	391
2-methylpyrid-3-yloxy 3-bromothieryl	390
2-methylpyrid-3-yloxy 2-acetoxypheyl	363
2-methylpyrid-3-yloxy 5-methylisoxazol-3-yl	310
2-methylpyrid-3-yloxy 2-(phenylthio)pyrid-3-yl	414
2-methylpyrid-3-yloxy 2-(trifluoromethoxy)phenyl	389
2-methylpyrid-3-yloxy 1-phenyl-5-propylpyrazin-4-yl	413
2-methylpyrid-3-yloxy 2-ethoxyphenyl	349

2-methylpyrid-3-yloxy 3-chlorothien-2-yl	346
2-methylpyrid-3-yloxy 1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	365
2-methylpyrid-3-yloxy 3,5-dichlorophenyl	374
2-methylpyrid-3-yloxy 2-(propylthio)pyridin-3-yl	380
2-methylpyrid-3-yloxy 2-(ethylthio)pyridin-3-yl	366
2-methylpyrid-3-yloxy 3-bromopyridin-5-yl	385
2-methylpyrid-3-yloxy 4-methyl-1,2,3-thiadiazol-5-yl	327
2-methylpyrid-3-yloxy 1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	365
2-methylpyrid-3-yloxy 3-chlorobenzo(b)thiophen-2-yl	396
2-methylpyrid-3-yloxy 4-chlorophenyl	340
2-methylpyrid-3-yloxy 4-methyl-2-phenyl-1,2,3-triazol-5-yl	386
2-methylpyrid-3-yloxy benzo(b)thiophen-2-yl	361
2-methylpyrid-3-yloxy 3,4-dimethylphenyl	333
2-methylpyrid-3-yloxy 2-(phenoxy)pyridin-3-yl	398
2-methylpyrid-3-yloxy 2-(methylthio)pyridin-3-yl	352
2-methylpyrid-3-yloxy 5-methyl-3-phenylisoxazol-4-yl	386
2-methylpyrid-3-yloxy 4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	409
2-methylpyrid-3-yloxy 2-chloro-6-methylpyridin-4-yl	355
2-methylpyrid-3-yloxy 3,5-dimethylisoxazol-4-yl	324
2-methylpyrid-3-yloxy 1-naphthyl	355
2-methylpyrid-3-yloxy 2-fluorophenyl	323

2-methylpyrid-3-yl oxy	4-propylphenyl	347
2-methylpyrid-3-yl oxy	4-(trifluoromethyl)phenyl	373
2-methylpyrid-3-yl oxy	3-fluorophenyl	323
2-methylpyrid-3-yl oxy	2,6-difluorophenyl	341
2-methylpyrid-3-yl oxy	2-chlorophenyl	340
2-methylpyrid-3-yl oxy	3-(chloromethyl)phenyl	354
2-methylpyrid-3-yl oxy	4-(2-(2-methyl)propyl)phenyl	361
2-methylpyrid-3-yl oxy	3-chlorophenyl	340
2-methylpyrid-3-yl oxy	2-nitrophenyl	350
2-methylpyrid-3-yl oxy	3,5-dimethoxyphenyl	365
2-methylpyrid-3-yl oxy	2,6-dichlorophenyl	374
2-methylpyrid-3-yl oxy	2,4-dichlorophenyl	374
2-methylpyrid-3-yl oxy	4-fluorophenyl	323
2-methylpyrid-3-yl oxy	4-butylphenyl	361
2-methylpyrid-3-yl oxy	2-methylphenyl	319
2-methylpyrid-3-yl oxy	phenyl	305
2-methylpyrid-3-yl oxy	4-ethylphenyl	333
2-methylpyrid-3-yl oxy	2,3-difluorophenyl	341
2-methylpyrid-3-yl oxy	2,6-dimethoxyphenyl	365
2-methylpyrid-3-yl oxy	3,4-difluorophenyl	341
2-methylpyrid-3-yl oxy	2,5-difluorophenyl	341
2-methylpyrid-3-yl oxy	4-ethoxyphenyl	349
2-methylpyrid-3-yl oxy	2,4,6-trichlorophenyl	409
2-methylpyrid-3-yl oxy	3-methylphenyl	319
2-methylpyrid-3-yl oxy	2-fluoro-5-(trifluoromethyl)phenyl	391
2-methylpyrid-3-yl oxy	3-methoxyphenyl	335

2-methylpyrid-3-yl oxy	thien-2-yl	311
2-methylpyrid-3-yl oxy	2-bromophenyl	384
2-methylpyrid-3-yl oxy	4-bromophenyl	384
2-methylpyrid-3-yl oxy	4-fluoro-3-(trifluoromethyl)phenyl	391
2-methylpyrid-3-yl oxy	3-(trifluoromethoxy)phenyl	389
2-methylpyrid-3-yl oxy	9-fluorenon-4-yl	407
2-methylpyrid-3-yl oxy	isoxazol-5-yl	296
2-methylpyrid-3-yl oxy	benzofuroxan-5-yl	363
2-methylpyrid-3-yl oxy	2-chloropyrid-3-yl	341
2-methylpyrid-3-yl oxy	3,5-difluorophenyl	341
2-methylpyrid-3-yl oxy	2-(4-methylphenoxy)pyridin-3-yl	412
2-methylpyrid-3-yl oxy	pyridin-4-yl	306
2-methylpyrid-3-yl oxy	anthraquinon-2-yl	435
2-methylpyrid-3-yl oxy	2-iodophenyl	411
4-chloro-2,5-dimethylphenoxy	3,4-dimethoxyphenyl	413
4-chloro-2,5-dimethylphenoxy	2-(trifluoromethyl)phenyl	421
4-chloro-2,5-dimethylphenoxy	2,4-difluorophenyl	389
4-chloro-2,5-dimethylphenoxy	3-(trifluoromethyl)phenyl	421
4-chloro-2,5-dimethylphenoxy	2-naphthyl	403
4-chloro-2,5-dimethylphenoxy	2-methoxyphenyl	484
4-chloro-2,5-dimethylphenoxy	3,4,5-trimethylphenyl	443

4-chloro-2,5-dimethylphenoxy	3,4-dichlorophenyl	422	4-chloro-2,5-dimethylphenoxy	1-(2-(2-methylpropyl)-3-methylpyrazol-5-yl	413
4-chloro-2,5-dimethylphenoxy	3-bromophenyl	432	4-chloro-2,5-dimethylphenoxy	3,5-dichlorophenyl	422
4-chloro-2,5-dimethylphenoxy	3-pyridyl	354	4-chloro-2,5-dimethylphenoxy	2-(propylthio)pyridin-3-yl	428
4-chloro-2,5-dimethylphenoxy	2-ethoxynaphth-1-yl	447	4-chloro-2,5-dimethylphenoxy	2-(ethylthio)pyridin-3-yl	414
4-chloro-2,5-dimethylphenoxy	2,3-dichlorophenyl	422	4-chloro-2,5-dimethylphenoxy	3-bromopyridin-5-yl	433
4-chloro-2,5-dimethylphenoxy	6-chloropyrid-3-yl	388	4-chloro-2,5-dimethylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	375
4-chloro-2,5-dimethylphenoxy	4-(trifluoromethoxy)phenyl	437	4-chloro-2,5-dimethylphenoxy	1-methyl-3-(2-(2-methylpropyl)pyrazol-5-yl	413
4-chloro-2,5-dimethylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	439	4-chloro-2,5-dimethylphenoxy	3-chlorobenzo[b]thiophen-2-yl	443
4-chloro-2,5-dimethylphenoxy	3-bromothieryl	438	4-chloro-2,5-dimethylphenoxy	4-chlorophenyl	397
4-chloro-2,5-dimethylphenoxy	2-acetoxyphenyl	411	4-chloro-2,5-dimethylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	434
4-chloro-2,5-dimethylphenoxy	5-methylisoxazol-3-yl	358	4-chloro-2,5-dimethylphenoxy	benzo[b]thiophen-2-yl	409
4-chloro-2,5-dimethylphenoxy	2-(phenylthio)pyrid-3-yl	462	4-chloro-2,5-dimethylphenoxy	3,4-dimethylphenyl	381
4-chloro-2,5-dimethylphenoxy	2-(trifluoromethoxy)phenyl	437	4-chloro-2,5-dimethylphenoxy	2-(phenoxy)pyridin-3-yl	446
4-chloro-2,5-dimethylphenoxy	1-phenyl-5-propylpyrazin-4-yl	461	4-chloro-2,5-dimethylphenoxy	2-(methylthio)pyridin-3-yl	400
4-chloro-2,5-dimethylphenoxy	2-ethoxyphenyl	397	4-chloro-2,5-dimethylphenoxy	5-methyl-3-phenylisoxazol-4-yl	434
4-chloro-2,5-dimethylphenoxy	3-chlorothieryl	393			

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4-chloro-2,5-dimethylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	456
4-chloro-2,5-dimethylphenoxy	2-chloro-6-methylpyridin-4-yl	402
4-chloro-2,5-dimethylphenoxy	3,5-dimethylisoxazol-4-yl	372
4-chloro-2,5-dimethylphenoxy	1-naphthyl	403
4-chloro-2,5-dimethylphenoxy	2-fluorophenyl	371
4-chloro-2,5-dimethylphenoxy	4-propylphenyl	395
4-chloro-2,5-dimethylphenoxy	3-fluorophenyl	371
4-chloro-2,5-dimethylphenoxy	2,6-difluorophenyl	389
4-chloro-2,5-dimethylphenoxy	2-chlorophenyl	387
4-chloro-2,5-dimethylphenoxy	3-(chloromethyl)phenyl	401
4-chloro-2,5-dimethylphenoxy	4-(2-(2-methyl)propyl)phenyl	409
4-chloro-2,5-dimethylphenoxy	3-chlorophenyl	387
4-chloro-2,5-dimethylphenoxy	3,5-dimethoxyphenyl	413
4-chloro-2,5-dimethylphenoxy	2,6-dichlorophenyl	422
4-chloro-2,5-dimethylphenoxy	2,4-dichlorophenyl	422

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4-chloro-2,5-dimethylphenoxy	4-fluorophenyl	371
4-chloro-2,5-dimethylphenoxy	4-butylphenyl	409
4-chloro-2,5-dimethylphenoxy	2-methylphenyl	367
4-chloro-2,5-dimethylphenoxy	phenyl	353
4-chloro-2,5-dimethylphenoxy	4-ethylphenyl	381
4-chloro-2,5-dimethylphenoxy	2,3-difluorophenyl	389
4-chloro-2,5-dimethylphenoxy	2,6-dimethoxyphenyl	413
4-chloro-2,5-dimethylphenoxy	3,4-difluorophenyl	389
4-chloro-2,5-dimethylphenoxy	2,5-difluorophenyl	389
4-chloro-2,5-dimethylphenoxy	4-ethoxyphenyl	397
4-chloro-2,5-dimethylphenoxy	2,4,6-trichlorophenyl	456
4-chloro-2,5-dimethylphenoxy	3-methylphenyl	367
4-chloro-2,5-dimethylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	439
4-chloro-2,5-dimethylphenoxy	3-methoxyphenyl	383
4-chloro-2,5-dimethylphenoxy	2-bromophenyl	432
4-chloro-2,5-dimethylphenoxy	4-bromophenyl	432

4-chloro-2,5-dimethylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	439	4-chloro-2,5-dimethylphenoxy	2,3-dichloropyridin-5-yl	423
4-chloro-2,5-dimethylphenoxy	3-(trifluoromethoxy)phenyl	437	4-chloro-2,5-dimethylphenoxy	1-naphthyl	417
4-chloro-2,5-dimethylphenoxy	9-fluorenon-4-yl	455	4-chloro-2,5-dimethylphenoxy	2,4-dimethoxyphenyl	413
4-chloro-2,5-dimethylphenoxy	isoxazol-5-yl	344	4-chloro-2,5-dimethylphenoxy	3,5-bis(trifluoromethyl)phenyl	489
4-chloro-2,5-dimethylphenoxy	benzofuroxan-5-yl	411	4-chloro-2,5-dimethylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	480
4-chloro-2,5-dimethylphenoxy	2-chloropyrid-3-yl	388	4-chloro-2,5-dimethylphenoxy	pentafluorophenyl	443
4-chloro-2,5-dimethylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	460	4-methoxyphenoxy	3,4-dimethoxyphenyl	380
4-chloro-2,5-dimethylphenoxy	pyridin-4-yl	354	4-methoxyphenoxy	2-(trifluoromethyl)phenyl	388
4-chloro-2,5-dimethylphenoxy	anthraquinon-2-yl	483	4-methoxyphenoxy	2,4-difluorophenyl	356
4-chloro-2,5-dimethylphenoxy	2-iodophenyl	479	4-methoxyphenoxy	3-(trifluoromethyl)phenyl	388
4-chloro-2,5-dimethylphenoxy	4-pentylphenyl	423	4-methoxyphenoxy	2-naphthyl	370
4-chloro-2,5-dimethylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	496	4-methoxyphenoxy	2-methoxyphenyl	350
4-chloro-2,5-dimethylphenoxy	2,6-dimethylphenyl	381	4-methoxyphenoxy	3,4,5-trimethylphenyl	410
4-chloro-2,5-dimethylphenoxy	2,5-dimethoxyphenyl	413	4-methoxyphenoxy	3,4-dichlorophenyl	389
4-chloro-2,5-dimethylphenoxy	2,5-dichloropyridin-3-yl	423	4-methoxyphenoxy	3-bromophenyl	399
4-chloro-2,5-dimethylphenoxy	2-chloro-6-methoxypyridin-4-yl	418	4-methoxyphenoxy	3-pyridyl	321
			4-methoxyphenoxy	2-ethoxynaphth-1-yl	414
			4-methoxyphenoxy	2,3-dichlorophenyl	389
			4-methoxyphenoxy	6-chloropyrid-3-yl	356
			4-methoxyphenoxy	4-(trifluoromethoxy)phenyl	404
			4-methoxyphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	406
			4-methoxyphenoxy	3-bromothieryl	405

4-methoxyphenoxy	2-acetoxyphenyl	378
4-methoxyphenoxy	5-methylisoxazol-3-yl	325
4-methoxyphenoxy	2-(phenylthio)pyrid-3-yl	429
4-methoxyphenoxy	2-(trifluoromethoxy)phenyl	404
4-methoxyphenoxy	1-phenyl-5-propylpyrazin-4-yl	428
4-methoxyphenoxy	2-ethoxyphenyl	364
4-methoxyphenoxy	3-chlorobenzen-2-yl	361
4-methoxyphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	380
4-methoxyphenoxy	3,5-dichlorophenyl	389
4-methoxyphenoxy	2-(propylthio)pyridin-3-yl	395
4-methoxyphenoxy	2-(ethylthio)pyridin-3-yl	381
4-methoxyphenoxy	3-bromopyridin-5-yl	400
4-methoxyphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	342
4-methoxyphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	380
4-methoxyphenoxy	3-chlorobenzo[b]thiophen-2-yl	411
4-methoxyphenoxy	4-chlorophenyl	355
4-methoxyphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	401
4-methoxyphenoxy	benzo[b]thiophen-2-yl	376
4-methoxyphenoxy	3,4-dimethylphenyl	348
4-methoxyphenoxy	2-(phenoxy)pyridin-3-yl	413
4-methoxyphenoxy	2-(methylthio)pyridin-3-yl	367
4-methoxyphenoxy	5-methyl-3-phenylisoxazol-4-yl	401

4-methoxyphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	424
4-methoxyphenoxy	2-chloro-6-methylpyridin-4-yl	370
4-methoxyphenoxy	3,5-dimethylisoxazol-4-yl	339
4-methoxyphenoxy	1-naphthyl	370
4-methoxyphenoxy	2-fluorophenyl	338
4-methoxyphenoxy	4-propylphenyl	362
4-methoxyphenoxy	3-fluorophenyl	338
4-methoxyphenoxy	2,6-difluorophenyl	356
4-methoxyphenoxy	2-chlorophenyl	355
4-methoxyphenoxy	3-(chloromethyl)phenyl	369
4-methoxyphenoxy	4-(2-(2-methyl)propyl)phenyl	376
4-methoxyphenoxy	3-chlorophenyl	355
4-methoxyphenoxy	3,5-dimethoxyphenyl	380
4-methoxyphenoxy	2,6-dichlorophenyl	389
4-methoxyphenoxy	2,4-dichlorophenyl	389
4-methoxyphenoxy	4-fluorophenyl	338
4-methoxyphenoxy	4-butylphenyl	376
4-methoxyphenoxy	2-methylphenyl	334
4-methoxyphenoxy	phenyl	320
4-methoxyphenoxy	4-ethylphenyl	348
4-methoxyphenoxy	2,3-difluorophenyl	356
4-methoxyphenoxy	2,6-dimethoxyphenyl	380
4-methoxyphenoxy	3,4-difluorophenyl	356
4-methoxyphenoxy	2,5-difluorophenyl	356
4-methoxyphenoxy	4-ethoxyphenyl	364

4-methoxyphenoxy	2,4,6-trichlorophenyl	424
4-methoxyphenoxy	3-methylphenyl	334
4-methoxyphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	406
4-methoxyphenoxy	3-methoxyphenyl	350
4-methoxyphenoxy	2-bromophenyl	399
4-methoxyphenoxy	4-bromophenyl	399
4-methoxyphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	406
4-methoxyphenoxy	3-(trifluoromethoxy)phenyl	404
4-methoxyphenoxy	9-fluorenon-4-yl	422
4-methoxyphenoxy	isoxazol-5-yl	311
4-methoxyphenoxy	benzofuroxan-5-yl	378
4-methoxyphenoxy	2-chloropyrid-3-yl	356
4-methoxyphenoxy	2-(4-methylphenoxy)pyridin-3-yl	427
4-methoxyphenoxy	pyridin-4-yl	321
4-methoxyphenoxy	anthraquinon-2-yl	450
4-methoxyphenoxy	2-iodophenyl	446
4-methoxyphenoxy	4-pentylphenyl	390
4-methoxyphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	464
4-methoxyphenoxy	2,6-dimethylphenyl	348
4-methoxyphenoxy	2,5-dimethoxyphenyl	380
4-methoxyphenoxy	2,5-dichloropyridin-3-yl	390
4-methoxyphenoxy	2-chloro-6-methoxypyridin-4-yl	386
4-methoxyphenoxy	2,3-dichloropyridin-5-yl	390
4-methoxyphenoxy	1-naphthyl	384

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4-methoxyphenoxy	2,4-dimethoxyphenyl	380
4-methoxyphenoxy	3,5-bis(trifluoromethyl)phenyl	456
4-methoxyphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	448
4-methoxyphenoxy	pentafluorophenyl	410
2-(2-propoxy)phenoxy	3,4-dimethoxyphenyl	408
2-(2-propoxy)phenoxy	2-(trifluoromethyl)phenyl	416
2-(2-propoxy)phenoxy	2,4-difluorophenyl	384
2-(2-propoxy)phenoxy	3-(trifluoromethyl)phenyl	416
2-(2-propoxy)phenoxy	2-naphthyl	398
2-(2-propoxy)phenoxy	2-methoxyphenyl	378
2-(2-propoxy)phenoxy	3,4,5-trimethylphenyl	438
2-(2-propoxy)phenoxy	3,4-dichlorophenyl	417
2-(2-propoxy)phenoxy	3-bromophenyl	427
2-(2-propoxy)phenoxy	3-pyridyl	349
2-(2-propoxy)phenoxy	2-ethoxynaphth-1-yl	442
2-(2-propoxy)phenoxy	2,3-dichlorophenyl	417
2-(2-propoxy)phenoxy	6-chloropyrid-3-yl	384
2-(2-propoxy)phenoxy	4-(trifluoromethoxy)phenyl	432
2-(2-propoxy)phenoxy	2-fluoro-4-(trifluoromethyl)phenyl	434
2-(2-propoxy)phenoxy	3-bromothieryl	433
2-(2-propoxy)phenoxy	2-acetoxyphenyl	406
2-(2-propoxy)phenoxy	5-methylisoxazol-3-yl	353
2-(2-propoxy)phenoxy	2-(phenylthio)pyrid-3-yl	458
2-(2-propoxy)phenoxy	2-(trifluoromethoxy)phenyl	432
2-(2-propoxy)phenoxy	1-phenyl-5-propylpyrazin-4-yl	457

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2-(2-propoxy) phenoxy	2-ethoxyphenyl	392
2-(2-propoxy) phenoxy	3-chlorothiophen-2-yl	389
2-(2-propoxy) phenoxy	1-(2-(2-methyl) propyl)-3-methylpyrazol-5-yl	408
2-(2-propoxy) phenoxy	3,5-dichlorophenyl	417
2-(2-propoxy) phenoxy	2-(propylthio)pyridin-3-yl	423
2-(2-propoxy) phenoxy	2-(ethylthio)pyridin-3-yl	409
2-(2-propoxy) phenoxy	3-bromopyridin-5-yl	428
2-(2-propoxy) phenoxy	4-methyl-1,2,3-thiadiazol-5-yl	370
2-(2-propoxy) phenoxy	1-methyl-3-(2-(2-methyl) propyl) pyrazol-5-yl	408
2-(2-propoxy) phenoxy	3-chlorobenzo[b]thiophen-2-yl	439
2-(2-propoxy) phenoxy	4-chlorophenyl	383
2-(2-propoxy) phenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	429
2-(2-propoxy) phenoxy	benzo[b]thiophen-2-yl	404
2-(2-propoxy) phenoxy	3,4-dimethylphenyl	376
2-(2-propoxy) phenoxy	2-(phenoxy)pyridin-3-yl	441
2-(2-propoxy) phenoxy	2-(methylthio)pyridin-3-yl	395
2-(2-propoxy) phenoxy	5-methyl-3-phenylisoxazol-4-yl	429
2-(2-propoxy) phenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	452
2-(2-propoxy) phenoxy	2-chloro-6-methylpyridin-4-yl	398
2-(2-propoxy) phenoxy	3,5-dimethylisoxazol-4-yl	367
2-(2-propoxy) phenoxy	1-naphthyl	398

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2-(2-propoxy) phenoxy	2-fluorophenyl	366
2-(2-propoxy) phenoxy	4-propylphenyl	390
2-(2-propoxy) phenoxy	3-fluorophenyl	366
2-(2-propoxy) phenoxy	2,6-difluorophenyl	384
2-(2-propoxy) phenoxy	2-chlorophenyl	383
2-(2-propoxy) phenoxy	3-(chloromethyl) phenyl	397
2-(2-propoxy) phenoxy	4-(2-(2-methyl) propyl) phenyl	404
2-(2-propoxy) phenoxy	3-chlorophenyl	383
2-(2-propoxy) phenoxy	3,5-dimethoxyphenyl	408
2-(2-propoxy) phenoxy	2,6-dichlorophenyl	417
2-(2-propoxy) phenoxy	2,4-dichlorophenyl	417
2-(2-propoxy) phenoxy	4-fluorophenyl	366
2-(2-propoxy) phenoxy	4-butylphenyl	404
2-(2-propoxy) phenoxy	2-methylphenyl	362
2-(2-propoxy) phenoxy	phenyl	348
2-(2-propoxy) phenoxy	4-ethylphenyl	376
2-(2-propoxy) phenoxy	2,3-difluorophenyl	384
2-(2-propoxy) phenoxy	2,6-dimethoxyphenyl	408
2-(2-propoxy) phenoxy	3,4-difluorophenyl	384
2-(2-propoxy) phenoxy	2,5-difluorophenyl	384
2-(2-propoxy) phenoxy	4-ethoxyphenyl	392
2-(2-propoxy) phenoxy	2,4,6-trichlorophenyl	452
2-(2-propoxy) phenoxy	3-methylphenyl	362
2-(2-propoxy) phenoxy	2-fluoro-5-(trifluoromethyl) phenyl	434
2-(2-propoxy) phenoxy	3-methoxyphenyl	378
2-(2-propoxy) phenoxy	2-bromophenyl	427

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2-(2-propoxy)phenoxy 4-bromophenyl 427
 2-(2-propoxy)phenoxy 4-fluoro-3-(trifluoromethyl)phenyl 434
 2-(2-propoxy)phenoxy 3-(trifluoromethoxy)phenyl 432
 2-(2-propoxy)phenoxy 9-fluorenon-4-yl 450
 2-(2-propoxy)phenoxy isoxazol-5-yl 339
 2-(2-propoxy)phenoxy benzofuroxan-5-yl 406
 2-(2-propoxy)phenoxy 2-chloropyrid-3-yl 384
 2-(2-propoxy)phenoxy 2-(4-methylphenoxy)pyridin-3-yl 455
 2-(2-propoxy)phenoxy pyridin-4-yl 349
 2-(2-propoxy)phenoxy anthraquinon-2-yl 478
 2-(2-propoxy)phenoxy 2-iodophenyl 474
 2-(2-propoxy)phenoxy 4-pentylphenyl 419
 2-(2-propoxy)phenoxy 2-(4-chlorophenylthio)pyridin-3-yl 492
 2-(2-propoxy)phenoxy 2,6-dimethylphenyl 376
 2-(2-propoxy)phenoxy 2,5-dimethoxyphenyl 408
 2-(2-propoxy)phenoxy 2,5-dichloropyridin-3-yl 418
 2-(2-propoxy)phenoxy 2-chloro-6-methoxypyridin-4-yl 414
 2-(2-propoxy)phenoxy 2,3-dichloropyridin-5-yl 418
 2-(2-propoxy)phenoxy 1-naphthyl 412
 2-(2-propoxy)phenoxy 2,4-dimethoxyphenyl 408
 2-(2-propoxy)phenoxy 3,5-bis(trifluoromethyl)phenyl 484
 2-(2-propoxy)phenoxy 2-(4-chlorophenoxy)pyridin-3-yl 476
 2-(2-propoxy)phenoxy pentafluorophenyl 438

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4-fluorophenoxy 3,4-dimethoxyphenyl 368
 4-fluorophenoxy 2-(trifluoromethyl)phenyl 376
 4-fluorophenoxy 2,4-difluorophenyl 344
 4-fluorophenoxy 3-(trifluoromethyl)phenyl 376
 4-fluorophenoxy 2-naphthyl 358
 4-fluorophenoxy 2-methoxyphenyl 338
 4-fluorophenoxy 3,4,5-trimethylphenyl 398
 4-fluorophenoxy 3,4-dichlorophenyl 377
 4-fluorophenoxy 3-bromophenyl 387
 4-fluorophenoxy 3-pyridyl 309
 4-fluorophenoxy 2-ethoxynaphth-1-yl 402
 4-fluorophenoxy 2,3-dichlorophenyl 377
 4-fluorophenoxy 6-chloropyrid-3-yl 344
 4-fluorophenoxy 4-(trifluoromethoxy)phenyl 392
 4-fluorophenoxy 2-fluoro-4-(trifluoromethyl)phenyl 394
 4-fluorophenoxy 3-bromothieryl 393
 4-fluorophenoxy 2-acetoxyphenyl 366
 4-fluorophenoxy 5-methylisoxazol-3-yl 313
 4-fluorophenoxy 2-(phenylthio)pyrid-3-yl 417
 4-fluorophenoxy 2-(trifluoromethoxy)phenyl 392
 4-fluorophenoxy 1-phenyl-5-propylpyrazin-4-yl 416
 4-fluorophenoxy 2-ethoxyphenyl 352
 4-fluorophenoxy 3-chlorothien-2-yl 349
 4-fluorophenoxy 1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl 368
 4-fluorophenoxy 3,5-dichlorophenyl 377

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4-fluorophenoxy	2-(propylthio)pyridin-3-yl	383
4-fluorophenoxy	2-(ethylthio)pyridin-3-yl	369
4-fluorophenoxy	3-bromopyridin-5-yl	388
4-fluorophenoxy	4-methyl-1,2,3-thiadiazol-5-yl	330
4-fluorophenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	368
4-fluorophenoxy	3-chlorobenzo[b]thiophen-2-yl	399
4-fluorophenoxy	4-chlorophenyl	343
4-fluorophenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	389
4-fluorophenoxy	benzo[b]thiophen-2-yl	364
4-fluorophenoxy	3,4-dimethylphenyl	336
4-fluorophenoxy	2-(phenoxyl)pyridin-3-yl	401
4-fluorophenoxy	2-(methylthio)pyridin-3-yl	355
4-fluorophenoxy	5-methyl-3-phenylisoxazol-4-yl	389
4-fluorophenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	412
4-fluorophenoxy	2-chloro-6-methylpyridin-4-yl	358
4-fluorophenoxy	3,5-dimethylisoxazol-4-yl	327
4-fluorophenoxy	1-naphthyl	358
4-fluorophenoxy	2-fluorophenyl	326
4-fluorophenoxy	4-propylphenyl	350
4-fluorophenoxy	3-fluorophenyl	326
4-fluorophenoxy	2,6-difluorophenyl	344
4-fluorophenoxy	2-chlorophenyl	343

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4-fluorophenoxy	3-(chloromethyl)phenyl	357
4-fluorophenoxy	4-(12-methyl)propyl)phenyl	364
4-fluorophenoxy	3-chlorophenyl	343
4-fluorophenoxy	3,5-dimethoxyphenyl	368
4-fluorophenoxy	2,6-dichlorophenyl	377
4-fluorophenoxy	2,4-dichlorophenyl	377
4-fluorophenoxy	4-fluorophenyl	326
4-fluorophenoxy	4-butylphenyl	364
4-fluorophenoxy	2-methylphenyl	322
4-fluorophenoxy	phenyl	308
4-fluorophenoxy	4-ethylphenyl	336
4-fluorophenoxy	2,3-difluorophenyl	344
4-fluorophenoxy	2,6-dimethoxyphenyl	368
4-fluorophenoxy	3,4-difluorophenyl	344
4-fluorophenoxy	2,5-difluorophenyl	344
4-fluorophenoxy	4-ethoxyphenyl	352
4-fluorophenoxy	2,4,6-trichlorophenyl	412
4-fluorophenoxy	3-methylphenyl	322
4-fluorophenoxy	2-fluoro-5-(trifluoromethyl)phenyl	394
4-fluorophenoxy	3-methoxyphenyl	338
4-fluorophenoxy	2-bromophenyl	387
4-fluorophenoxy	4-bromophenyl	387
4-fluorophenoxy	4-fluoro-3-(trifluoromethyl)phenyl	394
4-fluorophenoxy	3-(trifluoromethoxy)phenyl	392
4-fluorophenoxy	9-fluorenon-4-yl	410

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4-fluorophenoxy	isoxazol-5-yl	299
4-fluorophenoxy	benzofuroxan-5-yl	366
4-fluorophenoxy	2-chloropyridin-3-yl	344
4-fluorophenoxy	2-(4-methylphenoxy)pyridin-3-yl	415
4-fluorophenoxy	pyridin-4-yl	309
4-fluorophenoxy	anthraquinon-2-yl	438
4-fluorophenoxy	2-iodophenyl	434
4-fluorophenoxy	4-pentylphenyl	378
4-fluorophenoxy	2-(4-chlorophenylthio)pyridin-3-yl	452
4-fluorophenoxy	2,6-dimethylphenyl	336
4-fluorophenoxy	2,5-dimethoxyphenyl	368
4-fluorophenoxy	2,5-dichloropyridin-3-yl	378
4-fluorophenoxy	2-chloro-6-methoxypyridin-4-yl	374
4-fluorophenoxy	2,3-dichloropyridin-5-yl	378
4-fluorophenoxy	1-naphthyl	372
4-fluorophenoxy	2,4-dimethoxyphenyl	368
4-fluorophenoxy	3,5-bis(trifluoromethyl)phenyl	444
4-fluorophenoxy	2-(4-chlorophenoxy)pyridin-3-yl	436
4-fluorophenoxy	pentafluorophenyl	398
4-chlorophenoxy	3,4-dimethoxyphenyl	385
4-chlorophenoxy	2-(trifluoromethyl)phenyl	393
4-chlorophenoxy	2,4-difluorophenyl	361
4-chlorophenoxy	3-(trifluoromethyl)phenyl	393
4-chlorophenoxy	2-naphthyl	375

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4-chlorophenoxy	2-methoxyphenyl	355
4-chlorophenoxy	3,4,5-trimethylphenyl	415
4-chlorophenoxy	3,4-dichlorophenyl	394
4-chlorophenoxy	3-bromophenyl	404
4-chlorophenoxy	3-pyridyl	326
4-chlorophenoxy	2-ethoxynaphth-1-yl	419
4-chlorophenoxy	2,3-dichlorophenyl	394
4-chlorophenoxy	6-chloropyridin-3-yl	360
4-chlorophenoxy	4-(trifluoromethoxy)phenyl	409
4-chlorophenoxy	2-fluoro-4-(trifluoromethyl)phenyl	411
4-chlorophenoxy	3-bromothieryl	410
4-chlorophenoxy	2-acetoxyphenyl	383
4-chlorophenoxy	5-methylisoxazol-3-yl	330
4-chlorophenoxy	2-(phenylthio)pyridin-3-yl	434
4-chlorophenoxy	2-(trifluoromethoxy)phenyl	409
4-chlorophenoxy	1-phenyl-5-propylpyrazin-4-yl	433
4-chlorophenoxy	2-ethoxyphenyl	369
4-chlorophenoxy	3-chlorothieryl-2-yl	365
4-chlorophenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	385
4-chlorophenoxy	3,5-dichlorophenyl	394
4-chlorophenoxy	2-(propylthio)pyridin-3-yl	400
4-chlorophenoxy	2-(ethylthio)pyridin-3-yl	386
4-chlorophenoxy	3-bromopyridin-5-yl	405
4-chlorophenoxy	4-methyl-1,2,3-thiadiazol-5-yl	347

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4-chlorophenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	385
4-chlorophenoxy	3-chlorobenzo[b]thiophen-2-yl	415
4-chlorophenoxy	4-chlorophenyl	359
4-chlorophenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	406
4-chlorophenoxy	benzo[b]thiophen-2-yl	381
4-chlorophenoxy	3,4-dimethylphenyl	353
4-chlorophenoxy	2-(phenoxy)pyridin-3-yl	418
4-chlorophenoxy	2-(methylthio)pyridin-3-yl	372
4-chlorophenoxy	5-methyl-3-phenylisoxazol-4-yl	406
4-chlorophenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	428
4-chlorophenoxy	2-chloro-6-methylpyridin-4-yl	374
4-chlorophenoxy	3,5-dimethylisoxazol-4-yl	344
4-chlorophenoxy	1-naphthyl	375
4-chlorophenoxy	2-fluorophenyl	343
4-chlorophenoxy	4-propylphenyl	367
4-chlorophenoxy	3-fluorophenyl	343
4-chlorophenoxy	2,6-difluorophenyl	361
4-chlorophenoxy	2-chlorophenyl	359
4-chlorophenoxy	3-(chloromethyl)phenyl	373
4-chlorophenoxy	4-(2-(2-methyl)propyl)phenyl	381
4-chlorophenoxy	3-chlorophenyl	359

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4-chlorophenoxy	3,5-dimethoxyphenyl	385
4-chlorophenoxy	2,6-dichlorophenyl	394
4-chlorophenoxy	2,4-dichlorophenyl	394
4-chlorophenoxy	4-fluorophenyl	343
4-chlorophenoxy	4-butylphenyl	381
4-chlorophenoxy	2-methylphenyl	339
4-chlorophenoxy	phenyl	325
4-chlorophenoxy	4-ethylphenyl	353
4-chlorophenoxy	2,3-difluorophenyl	361
4-chlorophenoxy	2,6-dimethoxyphenyl	385
4-chlorophenoxy	3,4-difluorophenyl	361
4-chlorophenoxy	2,5-difluorophenyl	361
4-chlorophenoxy	4-ethoxyphenyl	369
4-chlorophenoxy	2,4,6-trichlorophenyl	428
4-chlorophenoxy	3-methylphenyl	339
4-chlorophenoxy	2-fluoro-5-(trifluoromethyl)phenyl	411
4-chlorophenoxy	3-methoxyphenyl	355
4-chlorophenoxy	2-bromophenyl	404
4-chlorophenoxy	4-bromophenyl	404
4-chlorophenoxy	4-fluoro-3-(trifluoromethyl)phenyl	411
4-chlorophenoxy	3-(trifluoromethoxy)phenyl	409
4-chlorophenoxy	9-fluorenon-4-yl	427
4-chlorophenoxy	isoxazol-5-yl	316
4-chlorophenoxy	benzofuroxan-5-yl	383
4-chlorophenoxy	2-chloropyrid-3-yl	360

4-chlorophenoxy	2-(4-methylphenoxy)pyridin-3-yl	432	2,4-difluorophenoxy	3,4-dichlorophenyl	395
4-chlorophenoxy	pyridin-4-yl	326	2,4-difluorophenoxy	3-bromophenyl	405
4-chlorophenoxy	anthraquinon-2-yl	455	2,4-difluorophenoxy	3-pyridyl	327
4-chlorophenoxy	2-iodophenyl	451	2,4-difluorophenoxy	2-ethoxynaphth-1-yl	420
4-chlorophenoxy	4-pentylphenyl	395	2,4-difluorophenoxy	2,3-dichlorophenyl	395
4-chlorophenoxy	2-(4-chlorophenylthio)pyridin-3-yl	468	2,4-difluorophenoxy	6-chloropyrid-3-yl	362
4-chlorophenoxy	2,6-dimethylphenyl	353	2,4-difluorophenoxy	4-(trifluoromethoxy)phenyl	410
4-chlorophenoxy	2,5-dimethoxyphenyl	385	2,4-difluorophenoxy	2-fluoro-4-(trifluoromethyl)phenyl	412
4-chlorophenoxy	2,5-dichloropyridin-3-yl	395	2,4-difluorophenoxy	3-bromothieryl	411
4-chlorophenoxy	2-chloro-6-methoxypyridin-4-yl	390	2,4-difluorophenoxy	2-acetoxyphenyl	384
4-chlorophenoxy	2,3-dichloropyridin-5-yl	395	2,4-difluorophenoxy	5-methylisoxazol-3-yl	331
4-chlorophenoxy	1-naphthyl	389	2,4-difluorophenoxy	2-(phenylthio)pyrid-3-yl	435
4-chlorophenoxy	2,4-dimethoxyphenyl	385	2,4-difluorophenoxy	2-(trifluoromethoxy)phenyl	410
4-chlorophenoxy	3,5-bis(trifluoromethyl)phenyl	461	2,4-difluorophenoxy	1-phenyl-5-propylpyrazin-4-yl	434
4-chlorophenoxy	2-(4-chlorophenoxy)pyridin-3-yl	452	2,4-difluorophenoxy	2-ethoxyphenyl	370
4-chlorophenoxy	pentafluorophenyl	415	2,4-difluorophenoxy	3-chlorothien-2-yl	367
2,4-difluorophenoxy	3,4-dimethoxyphenyl	386	2,4-difluorophenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	386
2,4-difluorophenoxy	2-(trifluoromethyl)phenyl	394	2,4-difluorophenoxy	3,5-dichlorophenyl	395
2,4-difluorophenoxy	2,4-difluorophenyl	362	2,4-difluorophenoxy	2-(propylthio)pyridin-3-yl	401
2,4-difluorophenoxy	3-(trifluoromethyl)phenyl	394	2,4-difluorophenoxy	2-(ethylthio)pyridin-3-yl	387
2,4-difluorophenoxy	2-naphthyl	376	2,4-difluorophenoxy	3-bromopyridin-5-yl	406
2,4-difluorophenoxy	2-methoxyphenyl	356	2,4-difluorophenoxy	4-methyl-1,2,3-thiadiazol-5-yl	348
2,4-difluorophenoxy	3,4,5-trimethylphenyl	416	2,4-difluorophenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	386

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2,4-di fluorophenoxy	3-chlorobenzo [b] thiophen-2-yl	417
2,4-di fluorophenoxy	4-chlorophenyl	361
2,4-di fluorophenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	407
2,4-di fluorophenoxy	benzo [b] thiophen-2-yl	382
2,4-di fluorophenoxy	3,4-dimethylphenyl	354
2,4-di fluorophenoxy	2-(phenoxyl)pyridin-3-yl	409
2,4-di fluorophenoxy	2-(methylthio)pyridin-3-yl	373
2,4-di fluorophenoxy	5-methyl-3-phenylisoxazol-4-yl	407
2,4-di fluorophenoxy	4-chloro-1,3-dimethylpyrazolo [3,4-b] pyridin-3-yl	430
2,4-di fluorophenoxy	2-chloro-6-methylpyridin-4-yl	376
2,4-di fluorophenoxy	3,5-dimethylisoxazol-4-yl	345
2,4-di fluorophenoxy	1-naphthyl	376
2,4-di fluorophenoxy	2-fluorophenyl	344
2,4-di fluorophenoxy	4-propylphenyl	368
2,4-di fluorophenoxy	3-fluorophenyl	344
2,4-di fluorophenoxy	2,6-di fluorophenyl	362
2,4-di fluorophenoxy	2-chlorophenyl	361
2,4-di fluorophenoxy	3-(chloromethyl)phenyl	375
2,4-di fluorophenoxy	4-(2-(2-methyl)propyl)phenyl	382
2,4-di fluorophenoxy	3-chlorophenyl	361
2,4-di fluorophenoxy	3,5-dimethoxyphenyl	386
2,4-di fluorophenoxy	2,6-dichlorophenyl	395

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2,4-di fluorophenoxy	2,4-dichlorophenyl	392
2,4-di fluorophenoxy	4-fluorophenyl	344
2,4-di fluorophenoxy	4-butylphenyl	382
2,4-di fluorophenoxy	2-methylphenyl	340
2,4-di fluorophenoxy	phenyl	326
2,4-di fluorophenoxy	4-ethylphenyl	354
2,4-di fluorophenoxy	2,3-difluorophenyl	362
2,4-di fluorophenoxy	2,6-dimethoxyphenyl	386
2,4-di fluorophenoxy	3,4-di fluorophenyl	362
2,4-di fluorophenoxy	2,5-di fluorophenyl	362
2,4-di fluorophenoxy	4-ethoxyphenyl	370
2,4-di fluorophenoxy	2,4,6-trichlorophenyl	430
2,4-di fluorophenoxy	3-methylphenyl	340
2,4-di fluorophenoxy	2-fluoro-5-(trifluoromethyl)phenyl	412
2,4-di fluorophenoxy	3-methoxyphenyl	356
2,4-di fluorophenoxy	2-bromophenyl	405
2,4-di fluorophenoxy	4-bromophenyl	405
2,4-di fluorophenoxy	4-fluoro-3-(trifluoromethyl)phenyl	412
2,4-di fluorophenoxy	3-(trifluoromethoxy)phenyl	410
2,4-di fluorophenoxy	9-fluorenon-4-yl	428
2,4-di fluorophenoxy	isoxazol-5-yl	317
2,4-di fluorophenoxy	benzofuroxan-5-yl	384
2,4-di fluorophenoxy	2-chloropyrid-3-yl	362
2,4-di fluorophenoxy	2-(4-methylphenoxyl)pyridin-3-yl	433
2,4-di fluorophenoxy	pyridin-4-yl	327

2,4-difluorophenoxy	anthraquinon-2-yl	456
2,4-difluorophenoxy	2-iodophenyl	452
2,4-difluorophenoxy	4-pentylphenyl	396
2,4-difluorophenoxy	2-(4-chlorophenylthio)pyridin-3-yl	470
2,4-difluorophenoxy	2,6-dimethylphenyl	354
2,4-difluorophenoxy	2,5-dimethoxyphenyl	386
2,4-difluorophenoxy	2,5-dichloropyridin-3-yl	396
2,4-difluorophenoxy	2-chloro-6-methoxypyridin-4-yl	392
2,4-difluorophenoxy	2,3-dichloropyridin-5-yl	396
2,4-difluorophenoxy	1-naphthyl	390
2,4-difluorophenoxy	2,4-dimethoxyphenyl	386
2,4-difluorophenoxy	3,5-bis(trifluoromethyl)phenyl	462
2,4-difluorophenoxy	2-(4-chlorophenoxy)pyridin-3-yl	454
2,4-difluorophenoxy	pentafluorophenyl	416
4-thiomethylphenoxy	3,4-dimethoxyphenyl	396
4-thiomethylphenoxy	2-(trifluoromethyl)phenyl	404
4-thiomethylphenoxy	2,4-difluorophenyl	372
4-thiomethylphenoxy	3-(trifluoromethyl)phenyl	404
4-thiomethylphenoxy	2-naphthyl	386
4-thiomethylphenoxy	2-methoxyphenyl	366
4-thiomethylphenoxy	3,4,5-trimethylphenyl	426
4-thiomethylphenoxy	3,4-dichlorophenyl	405
4-thiomethylphenoxy	3-bromophenyl	415
4-thiomethylphenoxy	3-pyridyl	337
4-thiomethylphenoxy	2-ethoxynaphth-1-yl	430

4-thiomethylphenoxy	2,3-dichlorophenyl	405
4-thiomethylphenoxy	6-chloropyrid-3-yl	372
4-thiomethylphenoxy	4-(trifluoromethoxy)phenyl	420
4-thiomethylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	422
4-thiomethylphenoxy	3-bromothieryl	421
4-thiomethylphenoxy	2-acetoxyphenyl	394
4-thiomethylphenoxy	5-methylisoxazol-3-yl	341
4-thiomethylphenoxy	2-(phenylthio)pyrid-3-yl	446
4-thiomethylphenoxy	2-(trifluoromethoxy)phenyl	420
4-thiomethylphenoxy	1-phenyl-5-propylpyrazin-4-yl	445
4-thiomethylphenoxy	2-ethoxyphenyl	380
4-thiomethylphenoxy	3-chlorothien-2-yl	377
4-thiomethylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	396
4-thiomethylphenoxy	3,5-dichlorophenyl	405
4-thiomethylphenoxy	2-(propylthio)pyridin-3-yl	412
4-thiomethylphenoxy	2-(ethylthio)pyridin-3-yl	397
4-thiomethylphenoxy	3-bromopyridin-5-yl	416
4-thiomethylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	358
4-thiomethylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	396
4-thiomethylphenoxy	3-chlorobenzo[b]thiophen-2-yl	427
4-thiomethylphenoxy	4-chlorophenyl	371
4-thiomethylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	417

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4-chloromethylphenoxy	benzo[b]chlorophen-2-yl	392
4-chloromethylphenoxy	3,4-dimethylphenyl	364
4-chloromethylphenoxy	2-(phenoxy)pyridin-3-yl	429
4-chloromethylphenoxy	2-(methylthio)pyridin-3-yl	383
4-chloromethylphenoxy	5-methyl-3-phenylisoxazol-4-yl	417
4-chloromethylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	440
4-chloromethylphenoxy	2-chloro-6-methylpyridin-4-yl	386
4-chloromethylphenoxy	3,5-dimethylisoxazol-4-yl	355
4-chloromethylphenoxy	1-naphthyl	386
4-chloromethylphenoxy	2-fluorophenyl	354
4-chloromethylphenoxy	4-propylphenyl	378
4-chloromethylphenoxy	3-fluorophenyl	354
4-chloromethylphenoxy	2,6-difluorophenyl	372
4-chloromethylphenoxy	2-chlorophenyl	371
4-chloromethylphenoxy	3-(chloromethyl)phenyl	385
4-chloromethylphenoxy	4-(2-(2-methyl)propyl)phenyl	392
4-chloromethylphenoxy	3-chlorophenyl	371
4-chloromethylphenoxy	3,5-dimethoxyphenyl	396
4-chloromethylphenoxy	2,6-dichlorophenyl	405
4-chloromethylphenoxy	2,4-dichlorophenyl	405
4-chloromethylphenoxy	4-fluorophenyl	354
4-chloromethylphenoxy	4-butylphenyl	392
4-chloromethylphenoxy	2-methylphenyl	350
4-chloromethylphenoxy	phenyl	336

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4-chloromethylphenoxy	4-ethylphenyl	364
4-chloromethylphenoxy	2,3-difluorophenyl	372
4-chloromethylphenoxy	2,6-dimethoxyphenyl	396
4-chloromethylphenoxy	3,4-difluorophenyl	372
4-chloromethylphenoxy	2,5-difluorophenyl	372
4-chloromethylphenoxy	4-ethoxyphenyl	380
4-chloromethylphenoxy	2,4,6-trichlorophenyl	440
4-chloromethylphenoxy	3-methylphenyl	350
4-chloromethylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	422
4-chloromethylphenoxy	3-methoxyphenyl	366
4-chloromethylphenoxy	2-bromophenyl	415
4-chloromethylphenoxy	4-bromophenyl	415
4-chloromethylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	422
4-chloromethylphenoxy	3-(trifluoromethoxy)phenyl	420
4-chloromethylphenoxy	9-fluorenon-4-yl	438
4-chloromethylphenoxy	isoxazol-5-yl	327
4-chloromethylphenoxy	benzofuroxan-5-yl	394
4-chloromethylphenoxy	2-chloropropylid-3-yl	372
4-chloromethylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	443
4-chloromethylphenoxy	pyridin-4-yl	337
4-chloromethylphenoxy	anthraquinon-2-yl	466
4-chloromethylphenoxy	2-iodophenyl	462
4-chloromethylphenoxy	4-phenylphenyl	407
4-chloromethylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	480
4-chloromethylphenoxy	2,6-dimethylphenyl	364

4-thiomethylphenoxy	2,5-dimethoxyphenyl	396
4-thiomethylphenoxy	2,5-dichloropyridin-3-yl	406
4-thiomethylphenoxy	2-chloro-6-methoxypyridin-4-yl	402
4-thiomethylphenoxy	2,3-dichloropyridin-5-yl	406
4-thiomethylphenoxy	1-naphthyl	400
4-thiomethylphenoxy	2,4-dimethoxyphenyl	396
4-thiomethylphenoxy	3,5-bis(trifluoromethyl)phenyl	372
4-thiomethylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	464
4-thiomethylphenoxy	pentafluorophenyl	426
4-(2-(2-methyl)propyl)phenoxy	3,4-dimethoxyphenyl	406
4-(2-(2-methyl)propyl)phenoxy	2-(trifluoromethyl)phenyl	414
4-(2-(2-methyl)propyl)phenoxy	2,4-difluorophenyl	382
4-(2-(2-methyl)propyl)phenoxy	3-(trifluoromethyl)phenyl	414
4-(2-(2-methyl)propyl)phenoxy	2-naphthyl	396
4-(2-(2-methyl)propyl)phenoxy	2-methoxyphenyl	376
4-(2-(2-methyl)propyl)phenoxy	3,4,5-trimethylphenyl	436
4-(2-(2-methyl)propyl)phenoxy	3,4-dichlorophenyl	415
4-(2-(2-methyl)propyl)phenoxy	3-bromophenyl	425

4-(2-(2-methyl)propyl)phenoxy	3-pyridyl	347
4-(2-(2-methyl)propyl)phenoxy	2-ethoxynaphth-1-yl	441
4-(2-(2-methyl)propyl)phenoxy	2,3-dichlorophenyl	415
4-(2-(2-methyl)propyl)phenoxy	6-chloropyrid-3-yl	382
4-(2-(2-methyl)propyl)phenoxy	4-(trifluoromethoxy)phenyl	430
4-(2-(2-methyl)propyl)phenoxy	2-fluoro-4-(trifluoromethyl)phenyl	432
4-(2-(2-methyl)propyl)phenoxy	3-bromothieryl	431
4-(2-(2-methyl)propyl)phenoxy	2-acetoxyphenyl	404
4-(2-(2-methyl)propyl)phenoxy	5-methylisoxazol-3-yl	351
4-(2-(2-methyl)propyl)phenoxy	2-(phenylthio)pyrid-3-yl	456
4-(2-(2-methyl)propyl)phenoxy	2-(trifluoromethoxy)phenyl	430
4-(2-(2-methyl)propyl)phenoxy	1-phenyl-5-propylpyrazin-4-yl	455
4-(2-(2-methyl)propyl)phenoxy	2-ethoxyphenyl	390
4-(2-(2-methyl)propyl)phenoxy	3-chlorothien-2-yl	387
4-(2-(2-methyl)propyl)phenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	406

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4-(2-(2-methyl)propyl)phenoxy	3,5-dichlorophenyl	415
4-(2-(2-methyl)propyl)phenoxy	2-(propylthio)pyridin-3-yl	422
4-(2-(2-methyl)propyl)phenoxy	2-(ethylthio)pyridin-3-yl	407
4-(2-(2-methyl)propyl)phenoxy	3-bromopyridin-5-yl	426
4-(2-(2-methyl)propyl)phenoxy	4-methyl-1,2,3-chladiazol-5-yl	368
4-(2-(2-methyl)propyl)phenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	406
4-(2-(2-methyl)propyl)phenoxy	3-chlorobenzo[b]thiophen-2-yl	437
4-(2-(2-methyl)propyl)phenoxy	4-chlorophenyl	381
4-(2-(2-methyl)propyl)phenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	427
4-(2-(2-methyl)propyl)phenoxy	benzo[b]thiophen-2-yl	402
4-(2-(2-methyl)propyl)phenoxy	3,4-dimethylphenyl	374
4-(2-(2-methyl)propyl)phenoxy	2-(phenoxy)pyridin-3-yl	439
4-(2-(2-methyl)propyl)phenoxy	2-(methylthio)pyridin-3-yl	393
4-(2-(2-methyl)propyl)phenoxy	5-methyl-3-phenylisoxazol-4-yl	427
4-(2-(2-methyl)propyl)phenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	450

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4-(2-(2-methyl)propyl)phenoxy	2-chloro-6-methylpyridin-4-yl	396
4-(2-(2-methyl)propyl)phenoxy	3,5-dimethylisoxazol-4-yl	365
4-(2-(2-methyl)propyl)phenoxy	1-naphthyl	396
4-(2-(2-methyl)propyl)phenoxy	2-fluorophenyl	364
4-(2-(2-methyl)propyl)phenoxy	4-propylphenyl	388
4-(2-(2-methyl)propyl)phenoxy	3-fluorophenyl	364
4-(2-(2-methyl)propyl)phenoxy	2,6-difluorophenyl	382
4-(2-(2-methyl)propyl)phenoxy	2-chlorophenyl	381
4-(2-(2-methyl)propyl)phenoxy	3-(chloromethyl)phenyl	395
4-(2-(2-methyl)propyl)phenoxy	4-(2-(2-methyl)propyl)phenyl	402
4-(2-(2-methyl)propyl)phenoxy	3-chlorophenyl	381
4-(2-(2-methyl)propyl)phenoxy	3,5-dimethoxyphenyl	406
4-(2-(2-methyl)propyl)phenoxy	2,6-dichlorophenyl	415
4-(2-(2-methyl)propyl)phenoxy	2,4-dichlorophenyl	415
4-(2-(2-methyl)propyl)phenoxy	4-fluorophenyl	364
4-(2-(2-methyl)propyl)phenoxy	4-butylphenyl	402

4-(2-(2-methyl)propyl)phenoxy	2-methylphenyl	360
4-(2-(2-methyl)propyl)phenoxy	phenyl	346
4-(2-(2-methyl)propyl)phenoxy	4-ethylphenyl	374
4-(2-(2-methyl)propyl)phenoxy	2,3-difluorophenyl	382
4-(2-(2-methyl)propyl)phenoxy	2,6-dimethoxyphenyl	406
4-(2-(2-methyl)propyl)phenoxy	3,4-difluorophenyl	382
4-(2-(2-methyl)propyl)phenoxy	2,5-difluorophenyl	382
4-(2-(2-methyl)propyl)phenoxy	4-ethoxyphenyl	390
4-(2-(2-methyl)propyl)phenoxy	2,4,6-trichlorophenyl	450
4-(2-(2-methyl)propyl)phenoxy	3-methylphenyl	360
4-(2-(2-methyl)propyl)phenoxy	2-fluoro-5-(trifluoromethyl)phenyl	432
4-(2-(2-methyl)propyl)phenoxy	3-methoxyphenyl	376
4-(2-(2-methyl)propyl)phenoxy	2-bromophenyl	425
4-(2-(2-methyl)propyl)phenoxy	4-bromophenyl	425
4-(2-(2-methyl)propyl)phenoxy	4-fluoro-3-(trifluoromethyl)phenyl	432
4-(2-(2-methyl)propyl)phenoxy	3-(trifluoromethoxy)phenyl	430

4-(2-(2-methyl)propyl)phenoxy	9-fluorenon-4-yl	448
4-(2-(2-methyl)propyl)phenoxy	isoxazol-5-yl	338
4-(2-(2-methyl)propyl)phenoxy	benzofuroxan-5-yl	404
4-(2-(2-methyl)propyl)phenoxy	2-chloropyridin-3-yl	382
4-(2-(2-methyl)propyl)phenoxy	2-(4-methylphenoxy)pyridin-3-yl	454
4-(2-(2-methyl)propyl)phenoxy	pyridin-4-yl	347
4-(2-(2-methyl)propyl)phenoxy	anthraquinon-2-yl	476
4-(2-(2-methyl)propyl)phenoxy	2-iodophenyl	472
4-(2-(2-methyl)propyl)phenoxy	4-pentylphenyl	417
4-(2-(2-methyl)propyl)phenoxy	2-(4-chlorophenylthio)pyridin-3-yl	490
4-(2-(2-methyl)propyl)phenoxy	2,6-dimethylphenyl	374
4-(2-(2-methyl)propyl)phenoxy	2,5-dimethoxyphenyl	406
4-(2-(2-methyl)propyl)phenoxy	2,5-dichloropyridin-3-yl	416
4-(2-(2-methyl)propyl)phenoxy	2-chloro-6-methoxypyridin-4-yl	412
4-(2-(2-methyl)propyl)phenoxy	2,3-dichloropyridin-5-yl	416
4-(2-(2-methyl)propyl)phenoxy	1-naphthyl	410

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4-(2-(2-methyl)propyl)phenoxy	2,4-dimethoxyphenyl	406
4-(2-(2-methyl)propyl)phenoxy	3,5-bis(trifluoromethyl)phenyl	482
4-(2-(2-methyl)propyl)phenoxy	2-(4-chlorophenoxy)pyridin-3-yl	474
4-(2-(2-methyl)propyl)phenoxy	pentafluorophenyl	436
2,3-dimethylphenoxy	3,4-dimethoxyphenyl	378
2,3-dimethylphenoxy	2-(trifluoromethyl)phenyl	386
2,3-dimethylphenoxy	2,4-difluorophenyl	354
2,3-dimethylphenoxy	3-(trifluoromethyl)phenyl	386
2,3-dimethylphenoxy	2-naphthyl	368
2,3-dimethylphenoxy	2-methoxyphenyl	348
2,3-dimethylphenoxy	3,4,5-trimethylphenyl	408
2,3-dimethylphenoxy	3,4-dichlorophenyl	387
2,3-dimethylphenoxy	3-bromophenyl	397
2,3-dimethylphenoxy	3-pyridyl	319
2,3-dimethylphenoxy	2-ethoxynaphth-1-yl	412
2,3-dimethylphenoxy	2,3-dichlorophenyl	387
2,3-dimethylphenoxy	6-chloropyrid-3-yl	354
2,3-dimethylphenoxy	4-(trifluoromethoxy)phenyl	402
2,3-dimethylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	404
2,3-dimethylphenoxy	3-bromothieryl	403
2,3-dimethylphenoxy	2-acetoxyphenyl	376
2,3-dimethylphenoxy	5-methylisoxazol-3-yl	323
2,3-dimethylphenoxy	2-(phenylthio)pyrid-3-yl	427
2,3-dimethylphenoxy	2-(trifluoromethoxy)phenyl	402

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2,3-dimethylphenoxy	1-phenyl-5-propylpyrazin-4-yl	426
2,3-dimethylphenoxy	2-ethoxyphenyl	362
2,3-dimethylphenoxy	3-chlorothien-2-yl	359
2,3-dimethylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	378
2,3-dimethylphenoxy	3,5-dichlorophenyl	387
2,3-dimethylphenoxy	2-(propylthio)pyridin-3-yl	393
2,3-dimethylphenoxy	2-(ethylthio)pyridin-3-yl	379
2,3-dimethylphenoxy	3-bromopyridin-5-yl	398
2,3-dimethylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	340
2,3-dimethylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	378
2,3-dimethylphenoxy	3-chlorobenzo[b]thiophen-2-yl	409
2,3-dimethylphenoxy	4-chlorophenyl	353
2,3-dimethylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	399
2,3-dimethylphenoxy	benzo[b]thiophen-2-yl	374
2,3-dimethylphenoxy	3,4-dimethylphenyl	346
2,3-dimethylphenoxy	2-(phenoxy)pyridin-3-yl	411
2,3-dimethylphenoxy	2-(methylthio)pyridin-3-yl	365
2,3-dimethylphenoxy	5-methyl-3-phenylisoxazol-4-yl	399
2,3-dimethylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	422
2,3-dimethylphenoxy	2-chloro-6-methylpyridin-4-yl	368

2,3-dimethylphenoxy	3,5-dimethylisoxazol-4-yl	337
2,3-dimethylphenoxy	1-naphthyl	368
2,3-dimethylphenoxy	2-fluorophenyl	336
2,3-dimethylphenoxy	4-propylphenyl	360
2,3-dimethylphenoxy	3-fluorophenyl	336
2,3-dimethylphenoxy	2,6-difluorophenyl	354
2,3-dimethylphenoxy	2-chlorophenyl	353
2,3-dimethylphenoxy	3-(chloromethyl)phenyl	368
2,3-dimethylphenoxy	4-(2-(2-methyl)propyl)phenyl	374
2,3-dimethylphenoxy	3-chlorophenyl	353
2,3-dimethylphenoxy	3,5-dimethoxyphenyl	378
2,3-dimethylphenoxy	2,6-dichlorophenyl	387
2,3-dimethylphenoxy	2,4-dichlorophenyl	387
2,3-dimethylphenoxy	4-fluorophenyl	336
2,3-dimethylphenoxy	4-butylphenyl	374
2,3-dimethylphenoxy	2-methylphenyl	332
2,3-dimethylphenoxy	phenyl	318
2,3-dimethylphenoxy	4-ethylphenyl	346
2,3-dimethylphenoxy	2,3-difluorophenyl	354
2,3-dimethylphenoxy	2,6-dimethoxyphenyl	378
2,3-dimethylphenoxy	3,4-difluorophenyl	354
2,3-dimethylphenoxy	2,5-difluorophenyl	354
2,3-dimethylphenoxy	4-ethoxyphenyl	362
2,3-dimethylphenoxy	2,4,6-trichlorophenyl	422
2,3-dimethylphenoxy	3-methylphenyl	332
2,3-dimethylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	404

2,3-dimethylphenoxy	3-methoxyphenyl	348
2,3-dimethylphenoxy	2-bromophenyl	397
2,3-dimethylphenoxy	4-bromophenyl	397
2,3-dimethylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	404
2,3-dimethylphenoxy	3-(trifluoromethoxy)phenyl	402
2,3-dimethylphenoxy	9-fluorenon-4-yl	420
2,3-dimethylphenoxy	isoxazol-5-yl	609
2,3-dimethylphenoxy	benzofuroxan-5-yl	376
2,3-dimethylphenoxy	2-chloropyridin-3-yl	354
2,3-dimethylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	425
2,3-dimethylphenoxy	pyridin-4-yl	319
2,3-dimethylphenoxy	anthraquinon-2-yl	448
2,3-dimethylphenoxy	2-iodophenyl	444
2,3-dimethylphenoxy	4-pentylphenyl	388
2,3-dimethylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	462
2,3-dimethylphenoxy	2,6-dimethylphenyl	346
2,3-dimethylphenoxy	2,5-dimethoxyphenyl	378
2,3-dimethylphenoxy	2,5-dichloropyridin-3-yl	388
2,3-dimethylphenoxy	2-chloro-6-methoxypyridin-4-yl	384
2,3-dimethylphenoxy	2,3-dichloropyridin-5-yl	388
2,3-dimethylphenoxy	1-naphthyl	382
2,3-dimethylphenoxy	2,4-dimethoxyphenyl	378
2,3-dimethylphenoxy	3,5-bis(trifluoromethyl)phenyl	454

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2,3-dimethylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	446
2,3-dimethylphenoxy	pentafluorophenyl	408
3,5-(bis-2-propyl)phenoxy	3,4-dimethoxyphenyl	434
3,5-(bis-2-propyl)phenoxy	2-(trifluoromethyl)phenyl	442
3,5-(bis-2-propyl)phenoxy	2,4-difluorophenyl	410
3,5-(bis-2-propyl)phenoxy	3-(trifluoromethyl)phenyl	442
3,5-(bis-2-propyl)phenoxy	2-naphthyl	425
3,5-(bis-2-propyl)phenoxy	2-methoxyphenyl	404
3,5-(bis-2-propyl)phenoxy	3,4,5-trimethylphenyl	465
3,5-(bis-2-propyl)phenoxy	3,4-dichlorophenyl	443
3,5-(bis-2-propyl)phenoxy	3-bromophenyl	453
3,5-(bis-2-propyl)phenoxy	3-pyridyl	375
3,5-(bis-2-propyl)phenoxy	2-ethoxynaphth-1-yl	469
3,5-(bis-2-propyl)phenoxy	2,3-dichlorophenyl	443
3,5-(bis-2-propyl)phenoxy	6-chloropyrid-3-yl	410
3,5-(bis-2-propyl)phenoxy	4-(trifluoromethoxy)phenyl	458

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3,5-(bis-2-propyl)phenoxy	2-fluoro-4-(trifluoromethyl)phenyl	460
3,5-(bis-2-propyl)phenoxy	3-bromothieryl	459
3,5-(bis-2-propyl)phenoxy	2-acetoxypheyl	432
3,5-(bis-2-propyl)phenoxy	5-methylisoxazol-3-yl	379
3,5-(bis-2-propyl)phenoxy	2-(phenylthio)pyrid-3-yl	484
3,5-(bis-2-propyl)phenoxy	2-(trifluoromethoxy)phenyl	458
3,5-(bis-2-propyl)phenoxy	1-phenyl-5-propylpyrazin-4-yl	483
3,5-(bis-2-propyl)phenoxy	2-ethoxyphenyl	418
3,5-(bis-2-propyl)phenoxy	3-chlorothiophen-2-yl	415
3,5-(bis-2-propyl)phenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	435
3,5-(bis-2-propyl)phenoxy	3,5-dichlorophenyl	443
3,5-(bis-2-propyl)phenoxy	2-(propylthio)pyridin-3-yl	450
3,5-(bis-2-propyl)phenoxy	2-(ethylthio)pyridin-3-yl	436
3,5-(bis-2-propyl)phenoxy	3-bromopyridin-5-yl	454
3,5-(bis-2-propyl)phenoxy	4-methyl-1,2,3-chiadiazol-5-yl	396
3,5-(bis-2-propyl)phenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	435

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3,5-(bis-2-propyl) phenoxy	3,4-difluorophenyl	410
3,5-(bis-2-propyl) phenoxy	2,5-difluorophenyl	410
3,5-(bis-2-propyl) phenoxy	4-ethoxyphenyl	418
3,5-(bis-2-propyl) phenoxy	2,4,6-trichlorophenyl	478
3,5-(bis-2-propyl) phenoxy	3-methylphenyl	388
3,5-(bis-2-propyl) phenoxy	2-fluoro-5-(trifluoromethyl) phenyl	460
3,5-(bis-2-propyl) phenoxy	3-methoxyphenyl	404
3,5-(bis-2-propyl) phenoxy	2-bromophenyl	453
3,5-(bis-2-propyl) phenoxy	4-bromophenyl	453
3,5-(bis-2-propyl) phenoxy	4-fluoro-3-(trifluoromethyl) phenyl	460
3,5-(bis-2-propyl) phenoxy	3-(trifluoromethoxy) phenyl	458
3,5-(bis-2-propyl) phenoxy	9-fluorenon-4-yl	477
3,5-(bis-2-propyl) phenoxy	isoxazol-5-yl	365
3,5-(bis-2-propyl) phenoxy	benzofuroxan-5-yl	432
3,5-(bis-2-propyl) phenoxy	2-chloropyrid-3-yl	410

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3,5-(bis-2-propyl) phenoxy	2-(4-methylphenoxy) pyridin-3-yl	482
3,5-(bis-2-propyl) phenoxy	pyridin-4-yl	375
3,5-(bis-2-propyl) phenoxy	anthraquinon-2-yl	505
3,5-(bis-2-propyl) phenoxy	2-iodophenyl	500
3,5-(bis-2-propyl) phenoxy	4-pentylphenyl	445
3,5-(bis-2-propyl) phenoxy	2-(4-chlorophenylthio) pyridin-3-yl	518
3,5-(bis-2-propyl) phenoxy	2,6-dimethylphenyl	402
3,5-(bis-2-propyl) phenoxy	2,5-dimethoxyphenyl	434
3,5-(bis-2-propyl) phenoxy	2,5-dichloropyridin-3-yl	444
3,5-(bis-2-propyl) phenoxy	2-chloro-6-methoxypyridin-4-yl	440
3,5-(bis-2-propyl) phenoxy	2,3-dichloropyridin-5-yl	444
3,5-(bis-2-propyl) phenoxy	1-naphthyl	439
3,5-(bis-2-propyl) phenoxy	2,4-dimethoxyphenyl	434
3,5-(bis-2-propyl) phenoxy	3,5-bis(trifluoromethyl) phenyl	510
3,5-(bis-2-propyl) phenoxy	2-(4-chlorophenoxy) pyridin-3-yl	502

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3,5-(bis-2-propyl)phenoxy	pentafluorophenyl	464	3-trifluoromethyl phenoxy	2-fluoro-4-(trifluoromethyl)phenyl	444
3-trifluoromethyl phenoxy	3,4-dimethoxyphenyl	418	3-trifluoromethyl phenoxy	3-bromothieryl	443
3-trifluoromethyl phenoxy	2-(trifluoromethyl)phenyl	426	3-trifluoromethyl phenoxy	2-acetoxyphenyl	416
3-trifluoromethyl phenoxy	2,4-difluorophenyl	394	3-trifluoromethyl phenoxy	5-methylisoxazol-3-yl	363
3-trifluoromethyl phenoxy	3-(trifluoromethyl)phenyl	426	3-trifluoromethyl phenoxy	2-(phenylthio)pyrid-3-yl	467
3-trifluoromethyl phenoxy	2-naphthyl	408	3-trifluoromethyl phenoxy	2-(trifluoromethoxy)phenyl	442
3-trifluoromethyl phenoxy	2-methoxyphenyl	388	3-trifluoromethyl phenoxy	1-phenyl-5-propylpyrazin-4-yl	466
3-trifluoromethyl phenoxy	3,4,5-trimethylphenyl	448	3-trifluoromethyl phenoxy	2-ethoxyphenyl	402
3-trifluoromethyl phenoxy	3,4-dichlorophenyl	427	3-trifluoromethyl phenoxy	3-chlorothieryl	399
3-trifluoromethyl phenoxy	3-bromophenyl	437	3-trifluoromethyl phenoxy	1-(2-(2-methylpropyl)-3-methylpyrazol-5-yl	418
3-trifluoromethyl phenoxy	3-pyridyl	359	3-trifluoromethyl phenoxy	3,5-dichlorophenyl	427
3-trifluoromethyl phenoxy	2-ethoxynaphth-1-yl	452	3-trifluoromethyl phenoxy	2-(propylthio)pyridin-3-yl	433
3-trifluoromethyl phenoxy	2,3-dichlorophenyl	427	3-trifluoromethyl phenoxy	2-(ethylthio)pyridin-3-yl	419
3-trifluoromethyl phenoxy	6-chloropyrid-3-yl	394	3-trifluoromethyl phenoxy	3-bromopyridin-5-yl	438
3-trifluoromethyl phenoxy	4-(trifluoromethoxy)phenyl	442	3-trifluoromethyl phenoxy	4-methyl-1,2,3-thiadiazol-5-yl	380

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3-trifluoromethyl phenoxy	1-methyl-3-(2-(2- methyl)propyl)pyrazol-5-yl	418
3-trifluoromethyl phenoxy	3-chlorobenzo[b]thiophen- 2-yl	449
3-trifluoromethyl phenoxy	4-chlorophenyl	393
3-trifluoromethyl phenoxy	4-methyl-2-phenyl-1,2,3- triazol-5-yl	439
3-trifluoromethyl phenoxy	benzo[b]thiophen-2-yl	414
3-trifluoromethyl phenoxy	3,4-dimethylphenyl	386
3-trifluoromethyl phenoxy	2-(phenoxy)pyridin-3-yl	451
3-trifluoromethyl phenoxy	2-(methylthio)pyridin-3-yl	405
3-trifluoromethyl phenoxy	5-methyl-3-phenylisoxazol- 4-yl	439
3-trifluoromethyl phenoxy	4-chloro-1,3-dimethyl pyrazolo[3,4-b]pyridin-3- yl	462
3-trifluoromethyl phenoxy	2-chloro-6-methylpyridin- 4-yl	408
3-trifluoromethyl phenoxy	3,5-dimethylisoxazol-4-yl	377
3-trifluoromethyl phenoxy	1-naphthyl	408
3-trifluoromethyl phenoxy	2-fluorophenyl	476
3-trifluoromethyl phenoxy	4-propylphenyl	400

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3-trifluoromethyl phenoxy	3-fluorophenyl	376
3-trifluoromethyl phenoxy	2,6-difluorophenyl	394
3-trifluoromethyl phenoxy	2-chlorophenyl	393
3-trifluoromethyl phenoxy	3-(chloromethyl)phenyl	407
3-trifluoromethyl phenoxy	4-(2-(2-methyl)propyl) phenyl	414
3-trifluoromethyl phenoxy	3-chlorophenyl	393
3-trifluoromethyl phenoxy	3,5-dimethoxyphenyl	418
3-trifluoromethyl phenoxy	2,6-dichlorophenyl	427
3-trifluoromethyl phenoxy	2,4-dichlorophenyl	427
3-trifluoromethyl phenoxy	4-fluorophenyl	376
3-trifluoromethyl phenoxy	4-butylphenyl	414
3-trifluoromethyl phenoxy	2-methylphenyl	372
3-trifluoromethyl phenoxy	phenyl	358
3-trifluoromethyl phenoxy	4-ethylphenyl	386
3-trifluoromethyl phenoxy	2,3-difluorophenyl	394
3-trifluoromethyl phenoxy	2,6-dimethoxyphenyl	418

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3-trifluoromethyl phenoxy	3,4-difluorophenyl	3-trifluoromethyl phenoxy	pyridin-4-yl
3-trifluoromethyl phenoxy	2,5-difluorophenyl	3-trifluoromethyl phenoxy	anthraquinon-2-yl
3-trifluoromethyl phenoxy	4-ethoxyphenyl	3-trifluoromethyl phenoxy	2-iodophenyl
3-trifluoromethyl phenoxy	2,4,6-trichlorophenyl	3-trifluoromethyl phenoxy	4-pentylphenyl
3-trifluoromethyl phenoxy	3-methylphenyl	3-trifluoromethyl phenoxy	2-(4-chlorophenylthio) pyridin-3-yl
3-trifluoromethyl phenoxy	2-fluoro-5- (trifluoromethyl)phenyl	3-trifluoromethyl phenoxy	2,6-dimethylphenyl
3-trifluoromethyl phenoxy	3-methoxyphenyl	3-trifluoromethyl phenoxy	2,5-dimethoxyphenyl
3-trifluoromethyl phenoxy	2-bromophenyl	3-trifluoromethyl phenoxy	2,5-dichloropyridin-3-yl
3-trifluoromethyl phenoxy	4-bromophenyl	3-trifluoromethyl phenoxy	2-chloro-6-methoxypyridin- 4-yl
3-trifluoromethyl phenoxy	4-fluoro-3- (trifluoromethyl)phenyl	3-trifluoromethyl phenoxy	2,3-dichloropyridin-5-yl
3-trifluoromethyl phenoxy	3-(trifluoromethoxy)phenyl	3-trifluoromethyl phenoxy	1-naphthyl
3-trifluoromethyl phenoxy	9-fluorenon-4-yl	3-trifluoromethyl phenoxy	2,4-dimethoxyphenyl
3-trifluoromethyl phenoxy	isoxazol-5-yl	3-trifluoromethyl phenoxy	3,5- bis(trifluoromethyl)phenyl
3-trifluoromethyl phenoxy	benzofuroxan-5-yl	3-trifluoromethyl phenoxy	2-(4- chlorophenoxy)pyridin-3-yl
3-trifluoromethyl phenoxy	2-chloropyrid-3-yl	3-trifluoromethyl phenoxy	pentafluorophenyl
3-trifluoromethyl phenoxy	2-(4- methylphenoxy)pyridin-3-yl	2,6-dichlorophenoxy	3,4-dimethoxyphenyl

2,6-dichlorophenoxy	2-(trifluoromethyl)phenyl	427
2,6-dichlorophenoxy	2,4-difluorophenyl	395
2,6-dichlorophenoxy	3-(trifluoromethyl)phenyl	427
2,6-dichlorophenoxy	2-naphthyl	409
2,6-dichlorophenoxy	2-methoxyphenyl	389
2,6-dichlorophenoxy	3,4,5-trimethylphenyl	449
2,6-dichlorophenoxy	3,4-dichlorophenyl	428
2,6-dichlorophenoxy	3-bromophenyl	438
2,6-dichlorophenoxy	3-pyridyl	361
2,6-dichlorophenoxy	2-ethoxynaphth-1-yl	453
2,6-dichlorophenoxy	2,3-dichlorophenyl	428
2,6-dichlorophenoxy	6-chloropyrid-3-yl	395
2,6-dichlorophenoxy	4-(trifluoromethoxy)phenyl	443
2,6-dichlorophenoxy	2-fluoro-4-(trifluoromethyl)phenyl	445
2,6-dichlorophenoxy	3-bromothieryl	444
2,6-dichlorophenoxy	2-acetoxypheyl	417
2,6-dichlorophenoxy	5-methylisoxazol-3-yl	364
2,6-dichlorophenoxy	2-(phenylthio)pyrid-3-yl	468
2,6-dichlorophenoxy	2-(trifluoromethoxy)phenyl	443
2,6-dichlorophenoxy	1-phenyl-5-propylpyrazin-4-yl	467
2,6-dichlorophenoxy	2-ethoxyphenyl	403
2,6-dichlorophenoxy	3-chlorochlen-2-yl	400
2,6-dichlorophenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	419
2,6-dichlorophenoxy	3,5-dichlorophenyl	428
2,6-dichlorophenoxy	2-(propylthio)pyridin-3-yl	434

2,6-dichlorophenoxy	2-(ethylthio)pyridin-3-yl	420
2,6-dichlorophenoxy	3-bromopyridin-5-yl	439
2,6-dichlorophenoxy	4-methyl-1,2,3-thiadiazol-5-yl	381
2,6-dichlorophenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	419
2,6-dichlorophenoxy	3-chlorobenzo[b]thiophen-2-yl	450
2,6-dichlorophenoxy	4-chlorophenyl	394
2,6-dichlorophenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	440
2,6-dichlorophenoxy	benzo[b]thiophen-2-yl	415
2,6-dichlorophenoxy	3,4-dimethylphenyl	387
2,6-dichlorophenoxy	2-(phenoxy)pyridin-3-yl	452
2,6-dichlorophenoxy	2-(methylthio)pyridin-3-yl	406
2,6-dichlorophenoxy	5-methyl-3-phenylisoxazol-4-yl	440
2,6-dichlorophenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	463
2,6-dichlorophenoxy	2-chloro-6-methylpyridin-4-yl	409
2,6-dichlorophenoxy	3,5-dimethylisoxazol-4-yl	378
2,6-dichlorophenoxy	1-naphthyl	409
2,6-dichlorophenoxy	2-fluorophenyl	377
2,6-dichlorophenoxy	4-propylphenyl	401
2,6-dichlorophenoxy	3-fluorophenyl	377
2,6-dichlorophenoxy	2,6-difluorophenyl	395
2,6-dichlorophenoxy	2-chlorophenyl	394
2,6-dichlorophenoxy	3-(chloromethyl)phenyl	408

2, 6-dichlorophenoxy	4-(2-(2-methyl)propyl)phenyl	415	2, 6-dichlorophenoxy	benzofuroxan-5-yl	417
2, 6-dichlorophenoxy	3-chlorophenyl	694	2, 6-dichlorophenoxy	2-chloropyridin-3-yl	395
2, 6-dichlorophenoxy	3, 5-dimethoxyphenyl	419	2, 6-dichlorophenoxy	2-(4-methylphenoxy)pyridin-3-yl	466
2, 6-dichlorophenoxy	2, 6-dichlorophenyl	428	2, 6-dichlorophenoxy	pyridin-4-yl	360
2, 6-dichlorophenoxy	2, 4-dichlorophenyl	428	2, 6-dichlorophenoxy	anthraquinon-2-yl	489
2, 6-dichlorophenoxy	4-fluorophenyl	377	2, 6-dichlorophenoxy	2-iodophenyl	485
2, 6-dichlorophenoxy	4-butyphenyl	415	2, 6-dichlorophenoxy	4-pentylphenyl	429
2, 6-dichlorophenoxy	2-methylphenyl	373	2, 6-dichlorophenoxy	2-(4-chlorophenylthio)pyridin-3-yl	503
2, 6-dichlorophenoxy	phenyl	359	2, 6-dichlorophenoxy	2, 6-dimethylphenyl	387
2, 6-dichlorophenoxy	4-ethylphenyl	387	2, 6-dichlorophenoxy	2, 5-dimethoxyphenyl	419
2, 6-dichlorophenoxy	2, 3-difluorophenyl	395	2, 6-dichlorophenoxy	2, 5-dichloropyridin-3-yl	429
2, 6-dichlorophenoxy	2, 6-dimethoxyphenyl	419	2, 6-dichlorophenoxy	2-chloro-6-methoxypyridin-4-yl	425
2, 6-dichlorophenoxy	3, 4-difluorophenyl	395	2, 6-dichlorophenoxy	2, 3-dichloropyridin-5-yl	429
2, 6-dichlorophenoxy	2, 5-difluorophenyl	395	2, 6-dichlorophenoxy	1-naphthyl	413
2, 6-dichlorophenoxy	4-ethoxyphenyl	403	2, 6-dichlorophenoxy	2, 4-dimethoxyphenyl	419
2, 6-dichlorophenoxy	2, 4, 6-trichlorophenyl	463	2, 6-dichlorophenoxy	3, 5-bis(trifluoromethyl)phenyl	495
2, 6-dichlorophenoxy	3-methylphenyl	373	2, 6-dichlorophenoxy	2-(4-chlorophenoxy)pyridin-3-yl	487
2, 6-dichlorophenoxy	2-fluoro-5-(trifluoromethyl)phenyl	445	2, 6-dichlorophenoxy	pentafluorophenyl	449
2, 6-dichlorophenoxy	3-methoxyphenyl	389	2, 4-dichlorophenoxy	3, 4-dimethoxyphenyl	419
2, 6-dichlorophenoxy	2-bromophenyl	438	2, 4-dichlorophenoxy	2-(trifluoromethyl)phenyl	427
2, 6-dichlorophenoxy	4-bromophenyl	438	2, 4-dichlorophenoxy	2, 4-difluorophenyl	395
2, 6-dichlorophenoxy	4-fluoro-3-(trifluoromethyl)phenyl	445	2, 4-dichlorophenoxy	3-(trifluoromethyl)phenyl	427
2, 6-dichlorophenoxy	3-(trifluoromethoxy)phenyl	443	2, 4-dichlorophenoxy	2-naphthyl	409
2, 6-dichlorophenoxy	9-fluorenon-4-yl	461	2, 4-dichlorophenoxy	2-methoxyphenyl	389
2, 6-dichlorophenoxy	isoxazol-5-yl	350			

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2,4-dichlorophenoxy	3,4,5-trimethylphenyl	449
2,4-dichlorophenoxy	3,4-dichlorophenyl	428
2,4-dichlorophenoxy	3-bromophenyl	438
2,4-dichlorophenoxy	3-pyridyl	361
2,4-dichlorophenoxy	2-ethoxynaphth-1-yl	453
2,4-dichlorophenoxy	2,3-dichlorophenyl	428
2,4-dichlorophenoxy	6-chloropyrid-3-yl	395
2,4-dichlorophenoxy	4-(trifluoromethoxy)phenyl	443
2,4-dichlorophenoxy	2-fluoro-4-(trifluoromethyl)phenyl	445
2,4-dichlorophenoxy	3-bromothieryl	444
2,4-dichlorophenoxy	2-acetoxyphenyl	417
2,4-dichlorophenoxy	5-methylisoxazol-3-yl	364
2,4-dichlorophenoxy	2-(phenylthio)pyrid-3-yl	468
2,4-dichlorophenoxy	2-(trifluoromethoxy)phenyl	443
2,4-dichlorophenoxy	1-phenyl-5-propylpyrazin-4-yl	467
2,4-dichlorophenoxy	2-ethoxyphenyl	403
2,4-dichlorophenoxy	3-chlorothieryl-2-yl	400
2,4-dichlorophenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	419
2,4-dichlorophenoxy	3,5-dichlorophenyl	428
2,4-dichlorophenoxy	2-(propylthio)pyridin-3-yl	434
2,4-dichlorophenoxy	2-(ethylthio)pyridin-3-yl	420
2,4-dichlorophenoxy	3-bromopyridin-5-yl	439
2,4-dichlorophenoxy	4-methyl-1,2,3-thiadiazol-5-yl	381
2,4-dichlorophenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	419

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2,4-dichlorophenoxy	3-chlorobenzo[b]thiophen-2-yl	450
2,4-dichlorophenoxy	4-chlorophenyl	394
2,4-dichlorophenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	440
2,4-dichlorophenoxy	benzo[b]thiophen-2-yl	415
2,4-dichlorophenoxy	3,4-dimethylphenyl	387
2,4-dichlorophenoxy	2-(phenoxy)pyridin-3-yl	452
2,4-dichlorophenoxy	2-(methylthio)pyridin-3-yl	406
2,4-dichlorophenoxy	5-methyl-3-phenylisoxazol-4-yl	440
2,4-dichlorophenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	463
2,4-dichlorophenoxy	2-chloro-6-methylpyridin-4-yl	409
2,4-dichlorophenoxy	3,5-dimethylisoxazol-4-yl	378
2,4-dichlorophenoxy	1-naphthyl	409
2,4-dichlorophenoxy	2-fluorophenyl	377
2,4-dichlorophenoxy	4-propylphenyl	401
2,4-dichlorophenoxy	3-fluorophenyl	377
2,4-dichlorophenoxy	2,6-difluorophenyl	395
2,4-dichlorophenoxy	2-chlorophenyl	394
2,4-dichlorophenoxy	3-(chloromethyl)phenyl	408
2,4-dichlorophenoxy	4-(2-(2-methyl)propyl)phenyl	415
2,4-dichlorophenoxy	3-chlorophenyl	694
2,4-dichlorophenoxy	3,5-dimethoxyphenyl	419
2,4-dichlorophenoxy	2,6-dichlorophenyl	428

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2, 4-dichlorophenoxy	2, 4-dichlorophenyl	428	2, 4-dichlorophenoxy	anthraquinon-2-yl	489
2, 4-dichlorophenoxy	4-fluorophenyl	377	2, 4-dichlorophenoxy	2-iodophenyl	485
2, 4-dichlorophenoxy	4-butylphenyl	415	2, 4-dichlorophenoxy	4-pentylphenyl	429
2, 4-dichlorophenoxy	2-methylphenyl	373	2, 4-dichlorophenoxy	2-(4-chlorophenylthio) pyridin-3-yl	503
2, 4-dichlorophenoxy	phenyl	359	2, 4-dichlorophenoxy	2, 6-dimethylphenyl	387
2, 4-dichlorophenoxy	4-ethylphenyl	387	2, 4-dichlorophenoxy	2, 5-dimethoxyphenyl	419
2, 4-dichlorophenoxy	2, 3-difluorophenyl	395	2, 4-dichlorophenoxy	2, 5-dichloropyridin-3-yl	429
2, 4-dichlorophenoxy	2, 6-dimethoxyphenyl	419	2, 4-dichlorophenoxy	2-chloro-6-methoxypyridin- 4-yl	425
2, 4-dichlorophenoxy	3, 4-difluorophenyl	395	2, 4-dichlorophenoxy	2, 3-dichloropyridin-5-yl	429
2, 4-dichlorophenoxy	2, 5-difluorophenyl	395	2, 4-dichlorophenoxy	1-naphthyl	413
2, 4-dichlorophenoxy	4-ethoxyphenyl	403	2, 4-dichlorophenoxy	2, 4-dimethoxyphenyl	419
2, 4-dichlorophenoxy	2, 4, 6-trichlorophenyl	463	2, 4-dichlorophenoxy	3, 5- bis(trifluoromethyl)phenyl	495
2, 4-dichlorophenoxy	3-methylphenyl	373	2, 4-dichlorophenoxy	2-(4- chlorophenoxy)pyridin-3-yl	487
2, 4-dichlorophenoxy	2-fluoro-5- (trifluoromethyl)phenyl	445	2, 4-dichlorophenoxy	pentafluorophenyl	449
2, 4-dichlorophenoxy	3-methoxyphenyl	389	4-chloro-3- methylphenoxy	3, 4-dimethoxyphenyl	319
2, 4-dichlorophenoxy	2-bromophenyl	438	4-chloro-3- methylphenoxy	2-(trifluoromethyl)phenyl	407
2, 4-dichlorophenoxy	4-bromophenyl	438	4-chloro-3- methylphenoxy	2, 4-difluorophenyl	375
2, 4-dichlorophenoxy	4-fluoro-3- (trifluoromethyl)phenyl	445	4-chloro-3- methylphenoxy	3-(trifluoromethyl)phenyl	407
2, 4-dichlorophenoxy	3-(trifluoromethoxy)phenyl	443	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	9-fluorenon-4-yl	461	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	isoxazol-5-yl	350	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	benzofuroxan-5-yl	417	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	2-chloropyridin-3-yl	395	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	2-(4- methylphenoxy)pyridin-3-yl	466	4-chloro-3- methylphenoxy		
2, 4-dichlorophenoxy	pyridin-4-yl	360	4-chloro-3- methylphenoxy		

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4-chloro-3-methylphenoxy	3,4,5-trimethylphenyl	429
4-chloro-3-methylphenoxy	3,4-dichlorophenyl	408
4-chloro-3-methylphenoxy	3-bromophenyl	418
4-chloro-3-methylphenoxy	3-pyridyl	340
4-chloro-3-methylphenoxy	2-ethoxynaphth-1-yl	433
4-chloro-3-methylphenoxy	2,3-dichlorophenyl	408
4-chloro-3-methylphenoxy	6-chloropyrid-3-yl	374
4-chloro-3-methylphenoxy	4-(trifluoromethoxy)phenyl	423
4-chloro-3-methylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	425
4-chloro-3-methylphenoxy	3-bromothieryl	424
4-chloro-3-methylphenoxy	2-acetoxyphenyl	397
4-chloro-3-methylphenoxy	5-methylisoxazol-3-yl	344
4-chloro-3-methylphenoxy	2-(phenylthio)pyrid-3-yl	448
4-chloro-3-methylphenoxy	2-(trifluoromethoxy)phenyl	423
4-chloro-3-methylphenoxy	1-phenyl-5-propylpyrazin-4-yl	447
4-chloro-3-methylphenoxy	2-ethoxyphenyl	383

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4-chloro-3-methylphenoxy	3-chlorothieryl	379
4-chloro-3-methylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	399
4-chloro-3-methylphenoxy	3,5-dichlorophenyl	408
4-chloro-3-methylphenoxy	2-(propylthio)pyridin-3-yl	414
4-chloro-3-methylphenoxy	2-(ethylthio)pyridin-3-yl	400
4-chloro-3-methylphenoxy	3-bromopyridin-5-yl	419
4-chloro-3-methylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	361
4-chloro-3-methylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	399
4-chloro-3-methylphenoxy	3-chlorobenzo[b]thiophen-2-yl	429
4-chloro-3-methylphenoxy	4-chlorophenyl	373
4-chloro-3-methylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	420
4-chloro-3-methylphenoxy	benzo[b]thiophen-2-yl	395
4-chloro-3-methylphenoxy	3,4-dimethylphenyl	367
4-chloro-3-methylphenoxy	2-(phenoxy)pyridin-3-yl	432
4-chloro-3-methylphenoxy	2-(methylthio)pyridin-3-yl	386
4-chloro-3-methylphenoxy	5-methyl-3-phenylisoxazol-4-yl	420

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4-chloro-3-methylphenoxy	2-bromophenyl	418
4-chloro-3-methylphenoxy	4-bromophenyl	418
4-chloro-3-methylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	425
4-chloro-3-methylphenoxy	3-(trifluoromethoxy)phenyl	423
4-chloro-3-methylphenoxy	9-fluorenon-4-yl	441
4-chloro-3-methylphenoxy	isoxazol-5-yl	330
4-chloro-3-methylphenoxy	benzofuroxan-5-yl	397
4-chloro-3-methylphenoxy	2-chloropyrid-3-yl	374
4-chloro-3-methylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	446
4-chloro-3-methylphenoxy	pyridin-4-yl	340
4-chloro-3-methylphenoxy	anthraquinon-2-yl	469
4-chloro-3-methylphenoxy	2-iodophenyl	465
4-chloro-3-methylphenoxy	4-pentylphenyl	409
4-chloro-3-methylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	482
4-chloro-3-methylphenoxy	2,6-dimethylphenyl	367

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4-chloro-3-methylphenoxy	2,5-dimethoxyphenyl	399
4-chloro-3-methylphenoxy	2,5-dichloropyridin-3-yl	409
4-chloro-3-methylphenoxy	2-chloro-6-methoxypyridin-4-yl	404
4-chloro-3-methylphenoxy	2,3-dichloropyridin-5-yl	409
4-chloro-3-methylphenoxy	1-naphthyl	403
4-chloro-3-methylphenoxy	2,4-dimethoxyphenyl	399
4-chloro-3-methylphenoxy	3,5-bis(trifluoromethyl)phenyl	475
4-chloro-3-methylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	466
4-chloro-3-methylphenoxy	pentafluorophenyl	429
4-chloro-2-cyclohexylphenoxy	3,4-dimethoxyphenyl	467
4-chloro-2-cyclohexylphenoxy	2-(trifluoromethyl)phenyl	475
4-chloro-2-cyclohexylphenoxy	2,4-difluorophenyl	443
4-chloro-2-cyclohexylphenoxy	3-(trifluoromethyl)phenyl	475
4-chloro-2-cyclohexylphenoxy	2-naphthyl	457
4-chloro-2-cyclohexylphenoxy	2-methoxyphenyl	437

4-chloro-2-cyclohexylphenoxy	3,4,5-trimethylphenyl	497	4-chloro-2-cyclohexylphenoxy	2-ethoxyphenyl	451
4-chloro-2-cyclohexylphenoxy	3,4-dichlorophenyl	176	4-chloro-2-cyclohexylphenoxy	3-chlorothiophen-2-yl	447
4-chloro-2-cyclohexylphenoxy	3-bromophenyl	486	4-chloro-2-cyclohexylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	467
4-chloro-2-cyclohexylphenoxy	3-pyridyl	408	4-chloro-2-cyclohexylphenoxy	3,5-dichlorophenyl	476
4-chloro-2-cyclohexylphenoxy	2-ethoxynaphth-1-yl	501	4-chloro-2-cyclohexylphenoxy	2-(propylthio)pyridin-3-yl	482
4-chloro-2-cyclohexylphenoxy	2,3-dichlorophenyl	476	4-chloro-2-cyclohexylphenoxy	2-(ethylthio)pyridin-3-yl	468
4-chloro-2-cyclohexylphenoxy	6-chloropyridin-3-yl	442	4-chloro-2-cyclohexylphenoxy	3-bromopyridin-5-yl	487
4-chloro-2-cyclohexylphenoxy	4-(trifluoromethoxy)phenyl	491	4-chloro-2-cyclohexylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	429
4-chloro-2-cyclohexylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	493	4-chloro-2-cyclohexylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	467
4-chloro-2-cyclohexylphenoxy	3-bromothiophenyl	492	4-chloro-2-cyclohexylphenoxy	3-chlorobenzo[b]thiophen-2-yl	497
4-chloro-2-cyclohexylphenoxy	2-acetoxyphenyl	465	4-chloro-2-cyclohexylphenoxy	4-chlorophenyl	441
4-chloro-2-cyclohexylphenoxy	5-methylisoxazol-3-yl	412	4-chloro-2-cyclohexylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	488
4-chloro-2-cyclohexylphenoxy	2-(phenylthio)pyridin-3-yl	516	4-chloro-2-cyclohexylphenoxy	benzo[b]thiophen-2-yl	463
4-chloro-2-cyclohexylphenoxy	2-(trifluoromethoxy)phenyl	491	4-chloro-2-cyclohexylphenoxy	3,4-dimethylphenyl	435
4-chloro-2-cyclohexylphenoxy	1-phenyl-5-propylpyrazin-4-yl	515	4-chloro-2-cyclohexylphenoxy	2-(phenoxy)pyridin-3-yl	500

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4-chloro-2-cyclohexylphenoxy	2-(methylthio)pyridin-3-yl	454
4-chloro-2-cyclohexylphenoxy	5-methyl-3-phenylisoxazol-4-yl	488
4-chloro-2-cyclohexylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	510
4-chloro-2-cyclohexylphenoxy	2-chloro-6-methylpyridin-4-yl	456
4-chloro-2-cyclohexylphenoxy	3,5-dimethylisoxazol-4-yl	426
4-chloro-2-cyclohexylphenoxy	1-naphthyl	457
4-chloro-2-cyclohexylphenoxy	2-fluorophenyl	425
4-chloro-2-cyclohexylphenoxy	4-propylphenyl	449
4-chloro-2-cyclohexylphenoxy	3-fluorophenyl	425
4-chloro-2-cyclohexylphenoxy	2,6-difluorophenyl	443
4-chloro-2-cyclohexylphenoxy	2-chlorophenyl	441
4-chloro-2-cyclohexylphenoxy	3-(chloromethyl)phenyl	455
4-chloro-2-cyclohexylphenoxy	4-(2-(2-methyl)propyl)phenyl	463
4-chloro-2-cyclohexylphenoxy	3-chlorophenyl	441
4-chloro-2-cyclohexylphenoxy	3,5-dimethoxyphenyl	467

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4-chloro-2-cyclohexylphenoxy	2,6-dichlorophenyl	476
4-chloro-2-cyclohexylphenoxy	2,4-dichlorophenyl	476
4-chloro-2-cyclohexylphenoxy	4-fluorophenyl	425
4-chloro-2-cyclohexylphenoxy	4-butyphenyl	463
4-chloro-2-cyclohexylphenoxy	2-methylphenyl	421
4-chloro-2-cyclohexylphenoxy	phenyl	407
4-chloro-2-cyclohexylphenoxy	4-ethylphenyl	435
4-chloro-2-cyclohexylphenoxy	2,3-difluorophenyl	443
4-chloro-2-cyclohexylphenoxy	2,6-dimethoxyphenyl	467
4-chloro-2-cyclohexylphenoxy	3,4-difluorophenyl	443
4-chloro-2-cyclohexylphenoxy	2,5-difluorophenyl	443
4-chloro-2-cyclohexylphenoxy	4-ethoxyphenyl	451
4-chloro-2-cyclohexylphenoxy	2,4,6-trichlorophenyl	510
4-chloro-2-cyclohexylphenoxy	3-methylphenyl	421
4-chloro-2-cyclohexylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	493
4-chloro-2-cyclohexylphenoxy	3-methoxyphenyl	437

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4-chloro-2-cyclohexylphenoxy	2-bromophenyl	486	4-chloro-2-cyclohexylphenoxy	2,5-dichloropyridin-3-yl	477
4-chloro-2-cyclohexylphenoxy	4-bromophenyl	486	4-chloro-2-cyclohexylphenoxy	2-chloro-6-methoxypyridin-4-yl	472
4-chloro-2-cyclohexylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	493	4-chloro-2-cyclohexylphenoxy	2,3-dichloropyridin-5-yl	477
4-chloro-2-cyclohexylphenoxy	3-(trifluoromethoxy)phenyl	491	4-chloro-2-cyclohexylphenoxy	1-naphthyl	471
4-chloro-2-cyclohexylphenoxy	9-fluorenon-4-yl	503	4-chloro-2-cyclohexylphenoxy	2,4-dimethoxyphenyl	467
4-chloro-2-cyclohexylphenoxy	isoxazol-5-yl	398	4-chloro-2-cyclohexylphenoxy	3,5-bis(trifluoromethyl)phenyl	546
4-chloro-2-cyclohexylphenoxy	benzofuroxan-5-yl	465	4-chloro-2-cyclohexylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	534
4-chloro-2-cyclohexylphenoxy	2-chloropyrid-3-yl	442	4-chloro-2-cyclohexylphenoxy	pentafluorophenyl	497
4-chloro-2-cyclohexylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	514	4-chloro-3,5-dimethylphenoxy	3,4-dimethoxyphenyl	413
4-chloro-2-cyclohexylphenoxy	pyridin-4-yl	408	4-chloro-3,5-dimethylphenoxy	2-(trifluoromethyl)phenyl	421
4-chloro-2-cyclohexylphenoxy	anthraquinon-2-yl	537	4-chloro-3,5-dimethylphenoxy	2,4-difluorophenyl	389
4-chloro-2-cyclohexylphenoxy	2-iodophenyl	533	4-chloro-3,5-dimethylphenoxy	3-(trifluoromethyl)phenyl	421
4-chloro-2-cyclohexylphenoxy	4-pentylphenyl	477	4-chloro-3,5-dimethylphenoxy	2-naphthyl	403
4-chloro-2-cyclohexylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	550	4-chloro-3,5-dimethylphenoxy	2-methoxyphenyl	484
4-chloro-2-cyclohexylphenoxy	2,6-dimethylphenyl	435	4-chloro-3,5-dimethylphenoxy	3,4,5-trimethylphenyl	443
4-chloro-2-cyclohexylphenoxy	2,5-dimethoxyphenyl	467	4-chloro-3,5-dimethylphenoxy	3,4-dichlorophenyl	422

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4-chloro-3,5-dimethylphenoxy	3-bromophenyl	432
4-chloro-3,5-dimethylphenoxy	3-pyridyl	354
4-chloro-3,5-dimethylphenoxy	2-ethoxynaphth-1-yl	447
4-chloro-3,5-dimethylphenoxy	2,3-dichlorophenyl	422
4-chloro-3,5-dimethylphenoxy	6-chloropyrid-3-yl	388
4-chloro-3,5-dimethylphenoxy	4-(trifluoromethoxy)phenyl	437
4-chloro-3,5-dimethylphenoxy	2-fluoro-4-(trifluoromethyl)phenyl	439
4-chloro-3,5-dimethylphenoxy	3-bromothieryl	438
4-chloro-3,5-dimethylphenoxy	2-acetoxypheyl	411
4-chloro-3,5-dimethylphenoxy	5-methylisoxazol-3-yl	358
4-chloro-3,5-dimethylphenoxy	2-(phenylthio)pyrid-3-yl	462
4-chloro-3,5-dimethylphenoxy	2-(trifluoromethoxy)phenyl	437
4-chloro-3,5-dimethylphenoxy	1-phenyl-5-propylpyrazin-4-yl	461
4-chloro-3,5-dimethylphenoxy	2-ethoxyphenyl	397
4-chloro-3,5-dimethylphenoxy	3-chlorothien-2-yl	393
4-chloro-3,5-dimethylphenoxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	413

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4-chloro-3,5-dimethylphenoxy	3,5-dichlorophenyl	422
4-chloro-3,5-dimethylphenoxy	2-(propylthio)pyridin-3-yl	428
4-chloro-3,5-dimethylphenoxy	2-(ethylthio)pyridin-3-yl	414
4-chloro-3,5-dimethylphenoxy	3-bromopyridin-5-yl	433
4-chloro-3,5-dimethylphenoxy	4-methyl-1,2,3-thiadiazol-5-yl	375
4-chloro-3,5-dimethylphenoxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	413
4-chloro-3,5-dimethylphenoxy	3-chlorobenzo[b]thiophen-2-yl	443
4-chloro-3,5-dimethylphenoxy	4-chlorophenyl	387
4-chloro-3,5-dimethylphenoxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	434
4-chloro-3,5-dimethylphenoxy	benzo[b]thiophen-2-yl	409
4-chloro-3,5-dimethylphenoxy	3,4-dimethylphenyl	381
4-chloro-3,5-dimethylphenoxy	2-(phenoxy)pyridin-3-yl	446
4-chloro-3,5-dimethylphenoxy	2-(methylthio)pyridin-3-yl	400
4-chloro-3,5-dimethylphenoxy	5-methyl-3-phenylisoxazol-4-yl	434
4-chloro-3,5-dimethylphenoxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	456

4-chloro-3,5-dimethylphenoxy	2-chloro-6-methylpyridin-4-yl	402	4-chloro-3,5-dimethylphenoxy	4-butylphenyl	409
4-chloro-3,5-dimethylphenoxy	3,5-dimethylisoxazol-4-yl	372	4-chloro-3,5-dimethylphenoxy	2-methylphenyl	367
4-chloro-3,5-dimethylphenoxy	1-naphthyl	403	4-chloro-3,5-dimethylphenoxy	phenyl	353
4-chloro-3,5-dimethylphenoxy	2-fluorophenyl	371	4-chloro-3,5-dimethylphenoxy	4-ethylphenyl	381
4-chloro-3,5-dimethylphenoxy	4-propylphenyl	395	4-chloro-3,5-dimethylphenoxy	2,3-difluorophenyl	389
4-chloro-3,5-dimethylphenoxy	3-fluorophenyl	371	4-chloro-3,5-dimethylphenoxy	2,6-dimethoxyphenyl	413
4-chloro-3,5-dimethylphenoxy	2,6-difluorophenyl	389	4-chloro-3,5-dimethylphenoxy	3,4-difluorophenyl	389
4-chloro-3,5-dimethylphenoxy	2-chlorophenyl	387	4-chloro-3,5-dimethylphenoxy	2,5-difluorophenyl	389
4-chloro-3,5-dimethylphenoxy	3-(chloromethyl)phenyl	401	4-chloro-3,5-dimethylphenoxy	4-ethoxyphenyl	397
4-chloro-3,5-dimethylphenoxy	4-(2-(2-methyl)propyl)phenyl	409	4-chloro-3,5-dimethylphenoxy	2,4,6-trichlorophenyl	456
4-chloro-3,5-dimethylphenoxy	3-chlorophenyl	387	4-chloro-3,5-dimethylphenoxy	3-methylphenyl	367
4-chloro-3,5-dimethylphenoxy	3,5-dimethoxyphenyl	413	4-chloro-3,5-dimethylphenoxy	2-fluoro-5-(trifluoromethyl)phenyl	439
4-chloro-3,5-dimethylphenoxy	2,6-dichlorophenyl	422	4-chloro-3,5-dimethylphenoxy	3-methoxyphenyl	383
4-chloro-3,5-dimethylphenoxy	2,4-dichlorophenyl	422	4-chloro-3,5-dimethylphenoxy	2-bromophenyl	432
4-chloro-3,5-dimethylphenoxy	4-fluorophenyl	371	4-chloro-3,5-dimethylphenoxy	4-bromophenyl	432

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4-chloro-3,5-dimethylphenoxy	4-fluoro-3-(trifluoromethyl)phenyl	439
4-chloro-3,5-dimethylphenoxy	3-(trifluoromethoxy)phenyl	437
4-chloro-3,5-dimethylphenoxy	9-fluorenon-4-yl	455
4-chloro-3,5-dimethylphenoxy	isoxazol-5-yl	344
4-chloro-3,5-dimethylphenoxy	benzofuroxan-5-yl	411
4-chloro-3,5-dimethylphenoxy	2-chloropyrid-3-yl	388
4-chloro-3,5-dimethylphenoxy	2-(4-methylphenoxy)pyridin-3-yl	460
4-chloro-3,5-dimethylphenoxy	pyridin-4-yl	354
4-chloro-3,5-dimethylphenoxy	anthraquinon-2-yl	483
4-chloro-3,5-dimethylphenoxy	2-iodophenyl	479
4-chloro-3,5-dimethylphenoxy	4-pentylphenyl	423
4-chloro-3,5-dimethylphenoxy	2-(4-chlorophenylthio)pyridin-3-yl	496
4-chloro-3,5-dimethylphenoxy	2,6-dimethylphenyl	381
4-chloro-3,5-dimethylphenoxy	2,5-dimethoxyphenyl	413
4-chloro-3,5-dimethylphenoxy	2,5-dichloropyridin-3-yl	423

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4-chloro-3,5-dimethylphenoxy	2-chloro-6-methoxypyridin-4-yl	418
4-chloro-3,5-dimethylphenoxy	2,3-dichloropyridin-5-yl	423
4-chloro-3,5-dimethylphenoxy	1-naphthyl	417
4-chloro-3,5-dimethylphenoxy	2,4-dimethoxyphenyl	413
4-chloro-3,5-dimethylphenoxy	3,5-bis(trifluoromethyl)phenyl	489
4-chloro-3,5-dimethylphenoxy	2-(4-chlorophenoxy)pyridin-3-yl	480
4-chloro-3,5-dimethylphenoxy	pentacfluorophenyl	443
4-chloro-3,5-dimethylphenoxy	3,4-dimethoxyphenyl	351
4-chloro-3,5-dimethylphenoxy	2-(trifluoromethyl)phenyl	359
4-chloro-3,5-dimethylphenoxy	2,4-difluorophenyl	327
4-chloro-3,5-dimethylphenoxy	3-(trifluoromethyl)phenyl	359
4-chloro-3,5-dimethylphenoxy	2-naphthyl	341
4-chloro-3,5-dimethylphenoxy	2-methoxyphenyl	321
4-chloro-3,5-dimethylphenoxy	3,4,5-trimethylphenyl	381
4-chloro-3,5-dimethylphenoxy	3,4-dichlorophenyl	360
4-chloro-3,5-dimethylphenoxy	3-bromophenyl	370
4-chloro-3,5-dimethylphenoxy	3-pyridyl	292
4-chloro-3,5-dimethylphenoxy	2-ethoxynaphth-1-yl	385
4-chloro-3,5-dimethylphenoxy	2,3-dichlorophenyl	360
4-chloro-3,5-dimethylphenoxy	6-chloropyrid-3-yl	327
4-chloro-3,5-dimethylphenoxy	4-(trifluoromethoxy)phenyl	375

pyrid-3-yloxy	2-fluoro-4-(trifluoromethyl)phenyl	377	pyrid-3-yloxy	2-(methylthio)pyridin-3-yl	338
pyrid-3-yloxy	3-bromothieryl	376	pyrid-3-yloxy	5-methyl-3-phenylisoxazol-4-yl	372
pyrid-3-yloxy	2-acetoxyphenyl	349	pyrid-3-yloxy	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	395
pyrid-3-yloxy	5-methylisoxazol-3-yl	296	pyrid-3-yloxy	2-chloro-6-methylpyridin-4-yl	341
pyrid-3-yloxy	2-(phenylthio)pyrid-3-yl	400	pyrid-3-yloxy	3,5-dimethylisoxazol-4-yl	310
pyrid-3-yloxy	2-(trifluoromethoxy)phenyl	375	pyrid-3-yloxy	1-naphthyl	341
pyrid-3-yloxy	1-phenyl-5-propylpyrazin-4-yl	399	pyrid-3-yloxy	2-fluorophenyl	309
pyrid-3-yloxy	2-ethoxyphenyl	335	pyrid-3-yloxy	4-propylphenyl	333
pyrid-3-yloxy	3-chlorothien-2-yl	332	pyrid-3-yloxy	3-fluorophenyl	309
pyrid-3-yloxy	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	351	pyrid-3-yloxy	2,6-difluorophenyl	327
pyrid-3-yloxy	3,5-dichlorophenyl	360	pyrid-3-yloxy	2-chlorophenyl	326
pyrid-3-yloxy	2-(propylthio)pyridin-3-yl	366	pyrid-3-yloxy	3-(chloromethyl)phenyl	340
pyrid-3-yloxy	2-(ethylthio)pyridin-3-yl	352	pyrid-3-yloxy	4-(2-(2-methyl)propyl)phenyl	347
pyrid-3-yloxy	3-bromopyridin-5-yl	371	pyrid-3-yloxy	3-chlorophenyl	326
pyrid-3-yloxy	4-methyl-1,2,3-thiadiazol-5-yl	313	pyrid-3-yloxy	3,5-dimethoxyphenyl	351
pyrid-3-yloxy	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	351	pyrid-3-yloxy	2,6-dichlorophenyl	360
pyrid-3-yloxy	3-chlorobenzo[b]thiophen-2-yl	382	pyrid-3-yloxy	2,4-dichlorophenyl	360
pyrid-3-yloxy	4-chlorophenyl	326	pyrid-3-yloxy	4-fluorophenyl	309
pyrid-3-yloxy	4-methyl-2-phenyl-1,2,3-triazol-5-yl	372	pyrid-3-yloxy	4-butylphenyl	347
pyrid-3-yloxy	benzo[b]thiophen-2-yl	347	pyrid-3-yloxy	2-methylphenyl	305
pyrid-3-yloxy	3,4-dimethylphenyl	319	pyrid-3-yloxy	phenyl	291
pyrid-3-yloxy	2-(phenoxy)pyridin-3-yl	384	pyrid-3-yloxy	4-ethylphenyl	319
			pyrid-3-yloxy	2,3-difluorophenyl	327
			pyrid-3-yloxy	2,6-dimethoxyphenyl	351

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pyrid-3-ylloxy	3,4-difluorophenyl	327
pyrid-3-ylloxy	2,5-difluorophenyl	327
pyrid-3-ylloxy	4-ethoxyphenyl	335
pyrid-3-ylloxy	2,4,6-trichlorophenyl	395
pyrid-3-ylloxy	3-methylphenyl	305
pyrid-3-ylloxy	2-fluoro-5-(trifluoromethyl)phenyl	377
pyrid-3-ylloxy	3-methoxyphenyl	321
pyrid-3-ylloxy	2-bromophenyl	370
pyrid-3-ylloxy	4-bromophenyl	370
pyrid-3-ylloxy	4-fluoro-3-(trifluoromethyl)phenyl	377
pyrid-3-ylloxy	3-(trifluoromethoxy)phenyl	375
pyrid-3-ylloxy	9-fluorenon-4-yl	393
pyrid-3-ylloxy	isoxazol-5-yl	282
pyrid-3-ylloxy	benzofuroxan-5-yl	349
pyrid-3-ylloxy	2-chloropyrid-3-yl	327
pyrid-3-ylloxy	2-(4-methylphenoxy)pyridin-3-yl	398
pyrid-3-ylloxy	pyridin-4-yl	292
pyrid-3-ylloxy	anthraquinon-2-yl	421
pyrid-3-ylloxy	2-iodophenyl	417
pyrid-3-ylloxy	4-pentylphenyl	361
pyrid-3-ylloxy	2-(4-chlorophenylthio)pyridin-3-yl	435
pyrid-3-ylloxy	2,6-dimethylphenyl	319
pyrid-3-ylloxy	2,5-dimethoxyphenyl	354
pyrid-3-ylloxy	2,5-dichloropyridin-3-yl	361

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pyrid-3-ylloxy	2-chloro-6-methoxypyridin-4-yl	357
pyrid-3-ylloxy	2,3-dichloropyridin-5-yl	361
pyrid-3-ylloxy	1-naphthyl	355
pyrid-3-ylloxy	2,4-dimethoxyphenyl	351
pyrid-3-ylloxy	3,5-bis(trifluoromethyl)phenyl	427
pyrid-3-ylloxy	2-(4-chlorophenoxy)pyridin-3-yl	419
pyrid-3-ylloxy	pentafluorophenyl	381
pyrid-3-ylloxy	3,4-dimethoxyphenyl	429
pyrid-3-ylloxy	2-(trifluoromethyl)phenyl	437
pyrid-3-ylloxy	2,4-difluorophenyl	405
pyrid-3-ylloxy	3-(trifluoromethyl)phenyl	437
pyrid-3-ylloxy	2-naphthyl	419
pyrid-3-ylloxy	2-methoxyphenyl	399
pyrid-3-ylloxy	3,4,5-trimethylphenyl	459
pyrid-3-ylloxy	3,4-dichlorophenyl	438
pyrid-3-ylloxy	3-bromophenyl	448
pyrid-3-ylloxy	3-pyridyl	370
pyrid-3-ylloxy	2-ethoxynaphth-1-yl	463
pyrid-3-ylloxy	2,3-dichlorophenyl	438
pyrid-3-ylloxy	6-chloropyrid-3-yl	405
pyrid-3-ylloxy	4-(trifluoromethoxy)phenyl	453
pyrid-3-ylloxy	2-fluoro-4-(trifluoromethyl)phenyl	455
pyrid-3-ylloxy	4-bromophenoxy	454
pyrid-3-ylloxy	4-bromophenoxy	427

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4-bromophenoxy	5-methylisoxazol-3-yl	374	4-bromophenoxy	4-chloro-1,3-dimethyl	473
4-bromophenoxy	2-(phenylthio)pyrid-3-yl	478		pyrazolo[3,4-b]pyridin-3-	
4-bromophenoxy	2-(trifluoromethoxy)phenyl	453		yl	
4-bromophenoxy	1-phenyl-5-propylpyrazin-	477		2-chloro-6-methylpyridin-	419
	4-yl			4-yl	
4-bromophenoxy	2-ethoxyphenyl	413		3,5-dimethylisoxazol-4-yl	388
4-bromophenoxy	3-chlorothien-2-yl	410		1-naphthyl	419
4-bromophenoxy	1-(2-(2-methyl)propyl)-3-	429		2-fluorophenyl	387
	methylpyrazol-5-yl			4-propylphenyl	411
4-bromophenoxy	3,5-dichlorophenyl	438		4-propylphenyl	411
4-bromophenoxy	2-(propylthio)pyridin-3-yl	444		3-fluorophenyl	387
4-bromophenoxy	2-(ethylthio)pyridin-3-yl	430		2,6-difluorophenyl	405
4-bromophenoxy	3-bromopyridin-5-yl	449		2-chlorophenyl	414
4-bromophenoxy	4-methyl-1,2,3-thiadiazol-	391		3-(chloromethyl)phenyl	418
	5-yl			4-(2-(2-	425
4-bromophenoxy	1-methyl-3-(2-(2-	429		methyl)propyl)phenyl	
	methyl)propyl)pyrazol-5-yl			3-chlorophenyl	404
4-bromophenoxy	3-chlorobenzo[b]thiophen-	460		3,5-dimethoxyphenyl	429
	2-yl			2,6-dichlorophenyl	438
4-bromophenoxy	4-chlorophenyl	404		2,4-dichlorophenyl	438
4-bromophenoxy	4-methyl-2-phenyl-1,2,3-	450		4-fluorophenyl	387
	triazol-5-yl			4-butyphenyl	425
4-bromophenoxy	benzo[b]thiophen-2-yl	425		2-methylphenyl	383
4-bromophenoxy	3,4-dimethylphenyl	397		phenyl	369
4-bromophenoxy	2-(phenoxy)pyridin-3-yl	462		4-ethylphenyl	397
4-bromophenoxy	2-(methylthio)pyridin-3-yl	416		2,3-difluorophenyl	405
4-bromophenoxy	5-methyl-3-phenylisoxazol-	450		2,6-dimethoxyphenyl	429
	4-yl			3,4-difluorophenyl	405
				2,5-difluorophenyl	405

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4-bromophenoxy	4-ethoxyphenyl	413
4-bromophenoxy	2,4,6-trichlorophenyl	473
4-bromophenoxy	3-methylphenyl	383
4-bromophenoxy	2-fluoro-5-(trifluoromethyl)phenyl	455
4-bromophenoxy	3-methoxyphenyl	399
4-bromophenoxy	2-bromophenyl	448
4-bromophenoxy	4-bromophenyl	448
4-bromophenoxy	4-fluoro-3-(trifluoromethyl)phenyl	455
4-bromophenoxy	3-(trifluoromethoxy)phenyl	453
4-bromophenoxy	9-fluorenon-4-yl	471
4-bromophenoxy	isoxazol-5-yl	360
4-bromophenoxy	benzofuroxan-5-yl	427
4-bromophenoxy	2-chloropyrid-3-yl	360
4-bromophenoxy	2-(4-methylphenoxy)pyridin-3-yl	476
4-bromophenoxy	pyridin-4-yl	370
4-bromophenoxy	anthraquinon-2-yl	499
4-bromophenoxy	2-iodophenyl	495
4-bromophenoxy	4-pentylphenyl	439
4-bromophenoxy	2-(4-chlorophenylthio)pyridin-3-yl	513
4-bromophenoxy	2,6-dimethylphenyl	397
4-bromophenoxy	2,5-dimethoxyphenyl	429
4-bromophenoxy	2,5-dichloropyridin-3-yl	439
4-bromophenoxy	2-chloro-6-methoxypyridin-4-yl	435

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4-bromophenoxy	2,3-dichloropyridin-5-yl	439
4-bromophenoxy	1-naphthyl	433
4-bromophenoxy	2,4-dimethoxyphenyl	429
4-bromophenoxy	3,5-bis(trifluoromethyl)phenyl	505
4-bromophenoxy	2-(4-chlorophenoxy)pyridin-3-yl	497
4-bromophenoxy	pentafluorophenyl	459
4-bromophenoxy	4-biphenyl	431
4-bromophenoxy	3,4-dimethoxyphenyl	415
4-bromophenoxy	2-(trifluoromethyl)phenyl	423
4-bromophenoxy	2,4-difluorophenyl	391
4-bromophenoxy	4-chloro-2-methylphenylthio	380
4-bromophenoxy	4-cyanophenyl	423
4-bromophenoxy	3-(trifluoromethyl)phenyl	380
4-bromophenoxy	4-chloro-2-methylphenylthio	405
4-bromophenoxy	2-naphthyl	385
4-bromophenoxy	2-methoxyphenyl	445
4-bromophenoxy	3,4,5-trimethylphenyl	400
4-bromophenoxy	4-nitrophenyl	
4-bromophenoxy	methylphenylthio	

4-chloro-2-methylphenylthio	3,4-dichlorophenyl	424	4-chloro-2-methylphenylthio	1-phenyl-5-propylpyrazin-4-yl	463
4-chloro-2-methylphenylthio	5-nitrofuranyl	390	4-chloro-2-methylphenylthio	2-ethoxyphenyl	399
4-chloro-2-methylphenylthio	3-bromophenyl	434	4-chloro-2-methylphenylthio	3-chlorothiophen-2-yl	395
4-chloro-2-methylphenylthio	3-pyridyl	356	4-chloro-2-methylphenylthio	1-(2-(2-methylpropyl)-3-methylpyrazol-5-yl	415
4-chloro-2-methylphenylthio	2-ethoxynaphth-1-yl	449	4-chloro-2-methylphenylthio	3,5-dichlorophenyl	424
4-chloro-2-methylphenylthio	2,3-dichlorophenyl	424	4-chloro-2-methylphenylthio	2-(propylthio)pyridin-3-yl	430
4-chloro-2-methylphenylthio	3-nitrophenyl	400	4-chloro-2-methylphenylthio	2-(ethylthio)pyridin-3-yl	416
4-chloro-2-methylphenylthio	6-chloropyrid-3-yl	390	4-chloro-2-methylphenylthio	3-bromopyridin-5-yl	435
4-chloro-2-methylphenylthio	4-(trifluoromethoxy)phenyl	439	4-chloro-2-methylphenylthio	4-methyl-1,2,3-thiadiazol-5-yl	377
4-chloro-2-methylphenylthio	2-fluoro-4-(trifluoromethyl)phenyl	441	4-chloro-2-methylphenylthio	1-methyl-3-(2-(2-methylpropyl)pyrazol-5-yl	415
4-chloro-2-methylphenylthio	3-bromothieryl	440	4-chloro-2-methylphenylthio	3-chlorobenzo[b]thiophen-2-yl	445
4-chloro-2-methylphenylthio	2-acetoxyphenyl	413	4-chloro-2-methylphenylthio	4-chlorophenyl	389
4-chloro-2-methylphenylthio	5-methylisoxazol-3-yl	360	4-chloro-2-methylphenylthio	4-methyl-2-phenyl-1,2,3-triazol-5-yl	436
4-chloro-2-methylphenylthio	2-(phenylthio)pyrid-3-yl	464	4-chloro-2-methylphenylthio	benzo[b]thiophen-2-yl	411
4-chloro-2-methylphenylthio	2-(trifluoromethoxy)phenyl	439	4-chloro-2-methylphenylthio	3,4-dimethylphenyl	383

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4-chloro-2-methylphenylthio	2-(phenoxy)pyridin-3-yl	448
4-chloro-2-methylphenylthio	2-(methylthio)pyridin-3-yl	402
4-chloro-2-methylphenylthio	5-methyl-3-phenylisoxazol-4-yl	436
4-chloro-2-methylphenylthio	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	458
4-chloro-2-methylphenylthio	2-chloro-6-methylpyridin-4-yl	404
4-chloro-2-methylphenylthio	3,5-dimethylisoxazol-4-yl	374
4-chloro-2-methylphenylthio	1-naphthyl	405
4-chloro-2-methylphenylthio	2-fluorophenyl	373
4-chloro-2-methylphenylthio	4-propylphenyl	397
4-chloro-2-methylphenylthio	4-(trifluoromethyl)phenyl	423
4-chloro-2-methylphenylthio	3-fluorophenyl	373
4-chloro-2-methylphenylthio	2,6-difluorophenyl	391
4-chloro-2-methylphenylthio	2-chlorophenyl	389
4-chloro-2-methylphenylthio	3-(chloromethyl)phenyl	403
4-chloro-2-methylphenylthio	4-(2-(2-methyl)propyl)phenyl	411

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4-chloro-2-methylphenylthio	3-chlorophenyl	389
4-chloro-2-methylphenylthio	2-nitrophenyl	400
4-chloro-2-methylphenylthio	3,5-dimethoxyphenyl	415
4-chloro-2-methylphenylthio	2,6-dichlorophenyl	424
4-chloro-2-methylphenylthio	2,4-dichlorophenyl	424
4-chloro-2-methylphenylthio	4-fluorophenyl	373
4-chloro-2-methylphenylthio	4-butyphenyl	411
4-chloro-2-methylphenylthio	2-methylphenyl	369
4-chloro-2-methylphenylthio	phenyl	355
4-chloro-2-methylphenylthio	4-ethylphenyl	383
4-chloro-2-methylphenylthio	2,3-di fluorophenyl	391
4-chloro-2-methylphenylthio	2,6-dimethoxyphenyl	415
4-chloro-2-methylphenylthio	3,4-di fluorophenyl	391
4-chloro-2-methylphenylthio	2,5-di fluorophenyl	391
4-chloro-2-methylphenylthio	4-ethoxyphenyl	399
4-chloro-2-methylphenylthio	2,4,6-trichlorophenyl	458

169		170	
4-chloro-2-methylphenylthio	3-methylphenyl	4-chloro-2-methylphenylthio	2-iodophenyl
4-chloro-2-methylphenylthio	2-fluoro-5-(trifluoromethyl)phenyl	4-chloro-2-methylanilino	4-biphenyl
4-chloro-2-methylphenylthio	3-methoxyphenyl	4-chloro-2-methylanilino	3,4-dimethoxyphenyl
4-chloro-2-methylphenylthio	thien-2-yl	4-chloro-2-methylanilino	2-(trifluoromethyl)phenyl
4-chloro-2-methylphenylthio	2-bromophenyl	4-chloro-2-methylanilino	2,4-difluorophenyl
4-chloro-2-methylphenylthio	4-bromophenyl	4-chloro-2-methylanilino	4-cyanophenyl
4-chloro-2-methylphenylthio	4-fluoro-3-(trifluoromethyl)phenyl	4-chloro-2-methylanilino	3-(trifluoromethyl)phenyl
4-chloro-2-methylphenylthio	3-(trifluoromethoxy)phenyl	4-chloro-2-methylanilino	3-cyanophenyl
4-chloro-2-methylphenylthio	9-fluorenon-4-yl	4-chloro-2-methylanilino	2-naphthyl
4-chloro-2-methylphenylthio	isoxazol-5-yl	4-chloro-2-methylanilino	2-methoxyphenyl
4-chloro-2-methylphenylthio	benzofuroxan-5-yl	4-chloro-2-methylanilino	3,4,5-trimethylphenyl
4-chloro-2-methylphenylthio	2-chloropyrid-3-yl	4-chloro-2-methylanilino	4-nitrophenyl
4-chloro-2-methylphenylthio	3,5-difluorophenyl	4-chloro-2-methylanilino	3,4-dichlorophenyl
4-chloro-2-methylphenylthio	2-(4-methylphenoxy)pyridin-3-yl	4-chloro-2-methylanilino	5-nitrofuran-2-yl
4-chloro-2-methylphenylthio	pyridin-4-yl	4-chloro-2-methylanilino	3-bromophenyl
4-chloro-2-methylphenylthio	anthraquinon-2-yl	4-chloro-2-methylanilino	3-pyridyl

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4-chloro-2-methylanilino	2-ethoxynaphth-1-yl	432
4-chloro-2-methylanilino	2,3-dichlorophenyl	407
4-chloro-2-methylanilino	3-nitrophenyl	383
4-chloro-2-methylanilino	6-chloropyrid-3-yl	373
4-chloro-2-methylanilino	4-(trifluoromethoxy)phenyl	422
4-chloro-2-methylanilino	2-fluoro-4-(trifluoromethyl)phenyl	424
4-chloro-2-methylanilino	3-bromothieryl	423
4-chloro-2-methylanilino	2-acetoxypheyl	396
4-chloro-2-methylanilino	5-methylisoxazol-3-yl	343
4-chloro-2-methylanilino	2-(phenylthio)pyrid-3-yl	447
4-chloro-2-methylanilino	2-(trifluoromethoxy)phenyl	422
4-chloro-2-methylanilino	1-phenyl-5-propylpyrazin-4-yl	446
4-chloro-2-methylanilino	2-ethoxypheyl	382
4-chloro-2-methylanilino	3-chlorothien-2-yl	378
4-chloro-2-methylanilino	1-(2-(2-methyl)propyl)-3-methylpyrazol-5-yl	398
4-chloro-2-methylanilino	3,5-dichlorophenyl	407

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4-chloro-2-methylanilino	2-(propylthio)pyridin-3-yl	413
4-chloro-2-methylanilino	2-(ethylthio)pyridin-3-yl	399
4-chloro-2-methylanilino	3-bromopyridin-5-yl	418
4-chloro-2-methylanilino	4-methyl-1,2,3-thiadiazol-5-yl	360
4-chloro-2-methylanilino	1-methyl-3-(2-(2-methyl)propyl)pyrazol-5-yl	398
4-chloro-2-methylanilino	3-chlorobenzo[b]thiophen-2-yl	428
4-chloro-2-methylanilino	4-chlorophenyl	372
4-chloro-2-methylanilino	4-methyl-2-phenyl-1,2,3-triazol-5-yl	419
4-chloro-2-methylanilino	benzo[b]thiophen-2-yl	394
4-chloro-2-methylanilino	3,4-dimethylphenyl	366
4-chloro-2-methylanilino	2-(phenoxyl)pyridin-3-yl	431
4-chloro-2-methylanilino	2-(methylthio)pyridin-3-yl	385
4-chloro-2-methylanilino	5-methyl-3-phenylisoxazol-4-yl	419
4-chloro-2-methylanilino	4-chloro-1,3-dimethylpyrazolo[3,4-b]pyridin-3-yl	441
4-chloro-2-methylanilino	2-chloro-6-methylpyridin-4-yl	387

4-chloro-2-methylanilino	3,5-dimethylisoxazol-4-yl	357	4-chloro-2-methylanilino	4-fluorophenyl	356
4-chloro-2-methylanilino	1-naphthyl	388	4-chloro-2-methylanilino	4-butylphenyl	394
4-chloro-2-methylanilino	2-fluorophenyl	356	4-chloro-2-methylanilino	2-methylphenyl	352
4-chloro-2-methylanilino	4-propylphenyl	380	4-chloro-2-methylanilino	phenyl	338
4-chloro-2-methylanilino	4-(trifluoromethyl)phenyl	406	4-chloro-2-methylanilino	4-ethylphenyl	366
4-chloro-2-methylanilino	3-fluorophenyl	356	4-chloro-2-methylanilino	2,3-difluorophenyl	374
4-chloro-2-methylanilino	2,6-difluorophenyl	374	4-chloro-2-methylanilino	2,6-dimethoxyphenyl	398
4-chloro-2-methylanilino	2-chlorophenyl	372	4-chloro-2-methylanilino	3,4-difluorophenyl	374
4-chloro-2-methylanilino	3-(chloromethyl)phenyl	386	4-chloro-2-methylanilino	2,5-difluorophenyl	374
4-chloro-2-methylanilino	4-(2-(2-methyl)propyl)phenyl	394	4-chloro-2-methylanilino	4-ethoxyphenyl	382
4-chloro-2-methylanilino	3-chlorophenyl	372	4-chloro-2-methylanilino	2,4,6-trichlorophenyl	441
4-chloro-2-methylanilino	2-nitrophenyl	383	4-chloro-2-methylanilino	3-methylphenyl	352
4-chloro-2-methylanilino	3,5-dimethoxyphenyl	398	4-chloro-2-methylanilino	2-fluoro-5-(trifluoromethyl)phenyl	424
4-chloro-2-methylanilino	2,6-dichlorophenyl	407	4-chloro-2-methylanilino	3-methoxyphenyl	368
4-chloro-2-methylanilino	2,4-dichlorophenyl	407	4-chloro-2-methylanilino	thien-2-yl	344

4-chloro-2,5-dimethylphenoxy	thien-2-yl	4-(2-(2-methyl)propyl)phenoxy	3-nitrophenyl
4-chloro-2,5-dimethylphenoxy	3,5-difluorophenyl	4-(2-(2-methyl)propyl)phenoxy	4-(trifluoromethyl)phenyl
4-methoxyphenoxy	3,5-difluorophenyl	4-(2-(2-methyl)propyl)phenoxy	2-nitrophenyl
2-(2-propoxy)phenoxy	4-(trifluoromethyl)phenyl		
2,4-difluorophenoxy	thien-2-yl	4-(2-(2-methyl)propyl)phenoxy	thien-2-yl
2,4-difluorophenoxy	3,5-difluorophenyl	4-(2-(2-methyl)propyl)phenoxy	3,5-difluorophenyl
4-thiomethylphenoxy	4-biphenyl		
4-thiomethylphenoxy	4-cyanophenyl	2,3-dimethylphenoxy	4-biphenyl
4-thiomethylphenoxy	3-cyanophenyl	2,3-dimethylphenoxy	4-cyanophenyl
4-thiomethylphenoxy	4-nitrophenyl	2,3-dimethylphenoxy	3-cyanophenyl
4-thiomethylphenoxy	5-nitrofuran-2-yl	2,3-dimethylphenoxy	4-nitrophenyl
4-thiomethylphenoxy	3-nitrophenyl	2,3-dimethylphenoxy	5-nitrofuran-2-yl
4-thiomethylphenoxy	4-(trifluoromethyl)phenyl	2,3-dimethylphenoxy	3-nitrophenyl
4-thiomethylphenoxy	2-nitrophenyl	2,3-dimethylphenoxy	4-(trifluoromethyl)phenyl
4-thiomethylphenoxy	thien-2-yl	2,3-dimethylphenoxy	2-nitrophenyl
4-thiomethylphenoxy	3,5-difluorophenyl	2,3-dimethylphenoxy	thien-2-yl
4-(2-(2-methyl)propyl)phenoxy	4-biphenyl	2,3-dimethylphenoxy	3,5-difluorophenyl
4-(2-(2-methyl)propyl)phenoxy	4-cyanophenyl	3,5-(bis-2-propyl)phenoxy	4-biphenyl
4-(2-(2-methyl)propyl)phenoxy	3-cyanophenyl	3,5-(bis-2-propyl)phenoxy	4-cyanophenyl
4-(2-(2-methyl)propyl)phenoxy	4-nitrophenyl	3,5-(bis-2-propyl)phenoxy	3-cyanophenyl
4-(2-(2-methyl)propyl)phenoxy	5-nitrofuran-2-yl	3,5-(bis-2-propyl)phenoxy	4-nitrophenyl
4-(2-(2-methyl)propyl)phenoxy		3,5-(bis-2-propyl)phenoxy	5-nitrofuran-2-yl
4-(2-(2-methyl)propyl)phenoxy		3,5-(bis-2-propyl)phenoxy	3-nitrophenyl
4-(2-(2-methyl)propyl)phenoxy		3,5-(bis-2-propyl)phenoxy	4-(trifluoromethyl)phenyl
4-(2-(2-methyl)propyl)phenoxy		3,5-(bis-2-propyl)phenoxy	2-nitrophenyl

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3,5-(bis-2-propyl)phenoxy	thien-2-yl
3,5-(bis-2-propyl)phenoxy	3,5-difluorophenyl
3-trifluoromethyl phenoxy	4-biphenyl
3-trifluoromethyl phenoxy	4-cyanophenyl
3-trifluoromethyl phenoxy	3-cyanophenyl
3-trifluoromethyl phenoxy	4-nitrophenyl
3-trifluoromethyl phenoxy	5-nitrofuran-2-yl
3-trifluoromethyl phenoxy	3-nitrophenyl
3-trifluoromethyl phenoxy	4-(trifluoromethyl)phenyl
3-trifluoromethyl phenoxy	2-nitrophenyl
3-trifluoromethyl phenoxy	thien-2-yl
3-trifluoromethyl phenoxy	3,5-difluorophenyl
2,6-dichlorophenoxy	4-biphenyl
2,6-dichlorophenoxy	4-cyanophenyl
2,6-dichlorophenoxy	3-cyanophenyl
2,6-dichlorophenoxy	4-nitrophenyl
2,6-dichlorophenoxy	5-nitrofuran-2-yl
2,6-dichlorophenoxy	3-nitrophenyl
2,6-dichlorophenoxy	4-(trifluoromethyl)phenyl
2,6-dichlorophenoxy	2-nitrophenyl
2,6-dichlorophenoxy	thien-2-yl
2,6-dichlorophenoxy	3,5-difluorophenyl
2,4-dichlorophenoxy	4-biphenyl
2,4-dichlorophenoxy	4-cyanophenyl
2,4-dichlorophenoxy	3-cyanophenyl
2,4-dichlorophenoxy	4-nitrophenyl
2,4-dichlorophenoxy	5-nitrofuran-2-yl
2,4-dichlorophenoxy	3-nitrophenyl

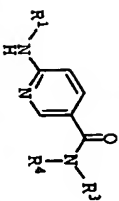
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2,4-dichlorophenoxy	4-(trifluoromethyl)phenyl
2,4-dichlorophenoxy	2-nitrophenyl
2,4-dichlorophenoxy	thien-2-yl
2,4-dichlorophenoxy	3,5-difluorophenyl
2,4-dichlorophenoxy	4-biphenyl
4-chloro-3-methylphenoxy	4-cyanophenyl
4-chloro-3-methylphenoxy	3-cyanophenyl
4-chloro-3-methylphenoxy	4-nitrophenyl
4-chloro-3-methylphenoxy	5-nitrofuran-2-yl
4-chloro-3-methylphenoxy	3-nitrophenyl
4-chloro-3-methylphenoxy	2-nitrophenyl
4-chloro-3-methylphenoxy	thien-2-yl
4-chloro-3-methylphenoxy	3,5-difluorophenyl
4-chloro-2-cyclohexylphenoxy	4-biphenyl
4-chloro-2-cyclohexylphenoxy	4-cyanophenyl
4-chloro-2-cyclohexylphenoxy	3-cyanophenyl
4-chloro-2-cyclohexylphenoxy	4-nitrophenyl
4-chloro-2-cyclohexylphenoxy	5-nitrofuran-2-yl
4-chloro-2-cyclohexylphenoxy	3-nitrophenyl
4-chloro-2-cyclohexylphenoxy	4-(trifluoromethyl)phenyl
4-chloro-2-cyclohexylphenoxy	2-nitrophenyl

4-chloro-2-cyclohexylphenoxy	thien-2-yl	pyrid-3-yloxy	4-(trifluoromethyl)phenyl
4-chloro-2-cyclohexylphenoxy	3,5-difluorophenyl	pyrid-3-yloxy	2-nitrophenyl
4-chloro-3,5-dimethylphenoxy	4-biphenyl	pyrid-3-yloxy	thien-2-yl
4-chloro-3,5-dimethylphenoxy	4-cyanophenyl	pyrid-3-yloxy	3,5-difluorophenyl
4-chloro-3,5-dimethylphenoxy	3-cyanophenyl	4-bromophenoxy	4-biphenyl
4-chloro-3,5-dimethylphenoxy	4-nitrophenyl	4-bromophenoxy	4-cyanophenyl
4-chloro-3,5-dimethylphenoxy	5-nitrofuran-2-yl	4-bromophenoxy	3-cyanophenyl
4-chloro-3,5-dimethylphenoxy	3-nitrophenyl	4-bromophenoxy	4-nitrophenyl
4-chloro-3,5-dimethylphenoxy	4-(trifluoromethyl)phenyl	4-bromophenoxy	5-nitrofuran-2-yl
4-chloro-3,5-dimethylphenoxy	2-nitrophenyl	4-bromophenoxy	3-nitrophenyl
4-chloro-3,5-dimethylphenoxy	thien-2-yl	4-bromophenoxy	4-(trifluoromethyl)phenyl
4-chloro-3,5-dimethylphenoxy	3,5-difluorophenyl	4-bromophenoxy	2-nitrophenyl
4-chloro-3,5-dimethylphenoxy	4-biphenyl	4-bromophenoxy	thien-2-yl
4-chloro-3,5-dimethylphenoxy	4-cyanophenyl	4-bromophenoxy	3,5-difluorophenyl
4-chloro-3,5-dimethylphenoxy	3-cyanophenyl	4-bromophenoxy	4-pentylphenyl
4-chloro-3,5-dimethylphenoxy	4-nitrophenyl	4-chloro-2-methylphenylthio	2-(4-chlorophenylthio)pyridin-3-yl
4-chloro-3,5-dimethylphenoxy	5-nitrofuran-2-yl	4-chloro-2-methylphenylthio	2,6-dimethylphenyl
4-chloro-3,5-dimethylphenoxy	3-nitrophenyl	4-chloro-2-methylphenylthio	2,5-dimethoxyphenyl
4-chloro-3,5-dimethylphenoxy	4-(trifluoromethyl)phenyl	4-chloro-2-methylphenylthio	2,5-dichloropyridin-3-yl
4-chloro-3,5-dimethylphenoxy	2-nitrophenyl	4-chloro-2-methylphenylthio	2-chloro-6-methoxypyridin-4-yl
4-chloro-3,5-dimethylphenoxy	thien-2-yl	4-chloro-2-methylphenylthio	2,3-dichloropyridin-5-yl
4-chloro-3,5-dimethylphenoxy	3,5-difluorophenyl	4-chloro-2-methylphenylthio	1-naphthyl
4-chloro-3,5-dimethylphenoxy	4-biphenyl	4-chloro-2-methylphenylthio	
4-chloro-3,5-dimethylphenoxy	4-cyanophenyl	4-chloro-2-methylphenylthio	
4-chloro-3,5-dimethylphenoxy	3-cyanophenyl	4-chloro-2-methylphenylthio	
4-chloro-3,5-dimethylphenoxy	4-nitrophenyl	4-chloro-2-methylphenylthio	
4-chloro-3,5-dimethylphenoxy	5-nitrofuran-2-yl	4-chloro-2-methylphenylthio	
4-chloro-3,5-dimethylphenoxy	3-nitrophenyl	4-chloro-2-methylphenylthio	

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4-chloro-2-methylphenylthio	2,4-dimethoxyphenyl
4-chloro-2-methylphenylthio	3,5-bis(trifluoromethyl)phenyl
4-chloro-2-methylphenylthio	2-(4-chlorophenoxy)pyridin-3-yl
4-chloro-2-methylphenylthio	pentafluorophenyl
4-chloro-2-methylphenylthio	4-pentylphenyl
4-chloro-2-methylphenylthio	2-(4-chlorophenylthio)pyridin-3-yl
4-chloro-2-methylphenylthio	2,6-dimethylphenyl
4-chloro-2-methylphenylthio	2,5-dimethoxyphenyl
4-chloro-2-methylphenylthio	2,5-dichloropyridin-3-yl
4-chloro-2-methylphenylthio	2-chloro-6-methoxypyridin-4-yl
4-chloro-2-methylphenylthio	2,3-dichloropyridin-5-yl
4-chloro-2-methylphenylthio	1-naphthyl
4-chloro-2-methylphenylthio	2,4-dimethoxyphenyl
4-chloro-2-methylphenylthio	3,5-bis(trifluoromethyl)phenyl
4-chloro-2-methylphenylthio	2-(4-chlorophenoxy)pyridin-3-yl
4-chloro-2-methylphenylthio	pentafluorophenyl

Example 19

General procedure for the synthesis of 6-(substituted-aminol)-N-substituted nicotinamides

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Step A. General procedure for the preparation of 6-chloro-N-substituted nicotinamide:

To a suspension of 6-chloronicotinoyl chloride (1.76 g, 10.0 mmol) in dry dichloromethane (10 mL) was added the amine (R¹R²NH) (10.0 mmol) followed by the dropwise addition of triethylamine (1.7 mL, 12.2 mmol). After stirring for 40 min. at room temperature, the mixture was diluted with dichloromethane, washed with aqueous 1 M hydrochloric acid, saturated aqueous sodium hydrogencarbonate and water, dried over sodium sulfate and concentrated to dryness under reduced pressure to afford the desired nicotinamide.

The following compounds were prepared according to this procedure using the appropriate substituted amine:

- 15 6-Chloro-N-o-tolylnicotinamide: MS (m/z): 247/249 (M⁺H)⁺; C₁₁H₉Cl₂N₂O, requires 246.5.
- 6-Chloro-N-(2-fluorophenyl)nicotinamide: MS (m/z): 251/253 (M⁺H)⁺; C₁₁H₇Cl₂F₂N₂O, requires 250.7.
- 20 6-Chloro-N-(2,6-dimethylphenyl)nicotinamide: MS (m/z): 261/263 (M⁺H)⁺; C₁₂H₁₃Cl₂N₂O, requires 260.7.
- 6-Chloro-N-(2-phenoxyphenyl)nicotinamide: MS (m/z): 325/327 (M⁺H)⁺; C₁₆H₁₃Cl₂N₂O, requires 324.8.
- 25 6-Chloro-N-phenylnicotinamide: MS (m/z): 233/235 (M⁺H)⁺; C₁₀H₈Cl₂N₂O, requires 232.7.
- 6-Chloro-N-(2,4-difluorophenyl)nicotinamide: MS (m/z): 269/271 (M⁺H)⁺; C₁₁H₇Cl₂F₂N₂O, requires 268.6.
- 6-Chloro-N-(2,6-disopropylphenyl)nicotinamide: MS (m/z): 317/319 (M⁺H)⁺; C₁₆H₂₁Cl₂N₂O, requires 316.8.
- 30 6-Chloro-N-(4-chlorophenyl)-N-methylnicotinamide: MS (m/z): 281/283 (M⁺H)⁺; C₁₁H₉Cl₂N₂O, requires 281.1.
- 6-Chloro-N-(2,4-dimethoxyphenyl)nicotinamide: MS (m/z): 293/295 (M⁺H)⁺; C₁₂H₁₃Cl₂N₂O, requires 292.7.
- 6-Chloro-N-(3-methoxyphenyl)nicotinamide: MS (m/z): 263/265 (M⁺H)⁺; C₁₁H₁₁Cl₂N₂O, requires 262.7.
- 35 6-Chloro-N-(4-methoxyphenyl)nicotinamide: MS (m/z): 263/265 (M⁺H)⁺; C₁₁H₁₁Cl₂N₂O, requires 262.7.

6-Chloro-N-(2-methoxyphenyl)nicotinamide: MS (m/z): 263/265 (M+H)⁺; C₁₁H₁₀Cl₁N₂O₂ requires 262.7.

6-Chloro-N-methyl-N-phenylnicotinamide: MS (m/z): 247/249 (M+H)⁺; C₁₁H₁₁Cl₁N₂O₂ requires 246.7.

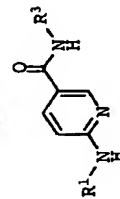
- 5 N-Benzyl-6-chloronicotinamide: MS (m/z): 247/249 (M+H)⁺; C₁₁H₁₀Cl₁N₂O₂ requires 246.7.

Step B. General procedure for the preparation of 6-(substituted-amino)-N-substituted nicotinamides

- 10 A mixture of the 6-chloro-N-substituted nicotinamide (12.5 mmol) and amine (R¹NH₂ or R¹NHCH₃) (20 mmol) in ethylene glycol (50 mL) or pyridine (alkylamines) (50 mL) was heated to 140°C for 20 hours. After cooling to room temperature, the mixture was diluted with dichloromethane/methanol (9:1, 250 mL) and filtered through a plug of silica gel, washing with additional dichloromethane/methanol (9:1, 250 mL). Concentration under reduced pressure afforded the desired 6-(substituted-amino)-N-substituted nicotinamide.
- 20 The compounds listed in Tables 8-11 were prepared from 6-chloro-N-substituted nicotinamides compounds and the appropriate amine according to the general procedure above.

25

Table 8



R ¹	R ³	MS (m/z)
o-tolyl	phenyl	303
o-tolyl	o-tolyl	317
o-tolyl	4-chloro-2-methylphenyl	352
o-tolyl	2-fluorophenyl	321

o-tolyl	3-fluorophenyl	321
o-tolyl	4-fluorophenyl	321
o-tolyl	2,4-difluorophenyl	339
o-tolyl	2-methoxyphenyl	333
o-tolyl	3-methoxyphenyl	333
o-tolyl	4-methoxyphenyl	333
o-tolyl	2,4-dimethoxyphenyl	363
o-tolyl	2-phenoxyphenyl	395
o-tolyl	3-phenoxyphenyl	395
o-tolyl	4-phenoxyphenyl	395
o-tolyl	4-biphenyl	379
o-tolyl	4-benzylphenyl	393
o-tolyl	4-(trifluoromethoxy)phenyl	387
o-tolyl	cyclohexyl	309
o-tolyl	2-methylcyclohexyl	323
o-tolyl	cycloheptyl	323
o-tolyl	indan-1-yl	343
o-tolyl	2-dicyclohexyl	492
2-fluorophenyl	phenyl	307
2-fluorophenyl	o-tolyl	321
2-fluorophenyl	4-chloro-2-methylphenyl	356
2-fluorophenyl	2-fluorophenyl	325
2-fluorophenyl	3-fluorophenyl	325
2-fluorophenyl	4-fluorophenyl	325
2-fluorophenyl	2,4-difluorophenyl	343
2-fluorophenyl	2-methoxyphenyl	337
2-fluorophenyl	3-methoxyphenyl	337
2-fluorophenyl	4-methoxyphenyl	337

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2-fluorophenyl	2, 4-dimethoxyphenyl	367
2-fluorophenyl	2-phenoxyphenyl	399
2-fluorophenyl	3-phenoxyphenyl	399
2-fluorophenyl	4-phenoxyphenyl	399
2-fluorophenyl	4-biphenyl	383
2-fluorophenyl	4-benzylphenyl	397
2-fluorophenyl	4-(trifluoromethoxy)phenyl	391
2-fluorophenyl	cyclohexyl	313
2-fluorophenyl	2-methylcyclohexyl	327
2-fluorophenyl	cycloheptyl	327
2-fluorophenyl	indan-1-yl	347
2-fluorophenyl	2-dicyclohexyl	395
2, 6-dimethylphenyl	phenyl	317
2, 6-dimethylphenyl	o-tolyl	331
2, 6-dimethylphenyl	4-chloro-2-methylphenyl	366
2, 6-dimethylphenyl	2-fluorophenyl	335
2, 6-dimethylphenyl	3-fluorophenyl	335
2, 6-dimethylphenyl	4-fluorophenyl	335
2, 6-dimethylphenyl	2, 4-difluorophenyl	353
2, 6-dimethylphenyl	2-methoxyphenyl	347
2, 6-dimethylphenyl	3-methoxyphenyl	347
2, 6-dimethylphenyl	4-methoxyphenyl	347
2, 6-dimethylphenyl	2, 4-dimethoxyphenyl	377
2, 6-dimethylphenyl	2-phenoxyphenyl	409
2, 6-dimethylphenyl	3-phenoxyphenyl	409
2, 6-dimethylphenyl	4-phenoxyphenyl	409
2, 6-dimethylphenyl	4-biphenyl	393
2, 6-dimethylphenyl	4-benzylphenyl	407

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2, 6-dimethylphenyl	4-(trifluoromethoxy)phenyl	401
2, 6-dimethylphenyl	cyclohexyl	323
2, 6-dimethylphenyl	2-methylcyclohexyl	337
2, 6-dimethylphenyl	cycloheptyl	667
2, 6-dimethylphenyl	indan-1-yl	357
2, 6-dimethylphenyl	2-dicyclohexyl	406
2-phenoxyphenyl	phenyl	381
2-phenoxyphenyl	o-tolyl	395
2-phenoxyphenyl	4-chloro-2-methylphenyl	430
2-phenoxyphenyl	2-fluorophenyl	399
2-phenoxyphenyl	3-fluorophenyl	399
2-phenoxyphenyl	4-fluorophenyl	399
2-phenoxyphenyl	2, 4-difluorophenyl	417
2-phenoxyphenyl	2-methoxyphenyl	411
2-phenoxyphenyl	3-methoxyphenyl	411
2-phenoxyphenyl	4-methoxyphenyl	411
2-phenoxyphenyl	2, 4-dimethoxyphenyl	441
2-phenoxyphenyl	2-phenoxyphenyl	473
2-phenoxyphenyl	3-phenoxyphenyl	473
2-phenoxyphenyl	4-phenoxyphenyl	473
2-phenoxyphenyl	4-biphenyl	457
2-phenoxyphenyl	4-benzylphenyl	472
2-phenoxyphenyl	4-(trifluoromethoxy)phenyl	465
2-phenoxyphenyl	cyclohexyl	387
2-phenoxyphenyl	2-methylcyclohexyl	401
2-phenoxyphenyl	cycloheptyl	401
2-phenoxyphenyl	indan-1-yl	421
2-phenoxyphenyl	2-dicyclohexyl	470

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phenyl	phenyl	289	2,4-difluorophenyl	2,4-difluorophenyl	361
phenyl	o-tolyl	303	2,4-difluorophenyl	2-methoxyphenyl	355
phenyl	4-chloro-2-methylphenyl	338	2,4-difluorophenyl	3-methoxyphenyl	355
phenyl	2-fluorophenyl	307	2,4-difluorophenyl	4-methoxyphenyl	355
phenyl	3-fluorophenyl	307	2,4-difluorophenyl	2,4-dimethoxyphenyl	385
phenyl	4-fluorophenyl	307	2,4-difluorophenyl	2-phenoxyphenyl	417
phenyl	2,4-difluorophenyl	325	2,4-difluorophenyl	3-phenoxyphenyl	417
phenyl	2-methoxyphenyl	319	2,4-difluorophenyl	4-phenoxyphenyl	417
phenyl	3-methoxyphenyl	319	2,4-difluorophenyl	4-biphenyl	401
phenyl	4-methoxyphenyl	319	2,4-difluorophenyl	4-benzylphenyl	415
phenyl	2,4-dimethoxyphenyl	349	2,4-difluorophenyl	4-(trifluoromethoxy)phenyl	409
phenyl	2-phenoxyphenyl	381	2,4-difluorophenyl	cyclohexyl	331
phenyl	3-phenoxyphenyl	381	2,4-difluorophenyl	2-methylcyclohexyl	345
phenyl	4-phenoxyphenyl	381	2,4-difluorophenyl	cycloheptyl	345
phenyl	4-biphenyl	365	2,4-difluorophenyl	indan-1-yl	365
phenyl	4-benzylphenyl	379	2,4-difluorophenyl	2-dicyclohexyl	413
phenyl	4-(trifluoromethoxy)phenyl	373	2,6-diisopropylphenyl	phenyl	373
phenyl	cyclohexyl	295	2,6-diisopropylphenyl	o-tolyl	387
phenyl	2-methylcyclohexyl	309	2,6-diisopropylphenyl	4-chloro-2-methylphenyl	422
phenyl	cycloheptyl	309	2,6-diisopropylphenyl	2-fluorophenyl	391
phenyl	indan-1-yl	329	2,6-diisopropylphenyl	3-fluorophenyl	391
phenyl	2-dicyclohexyl	377	2,6-diisopropylphenyl	4-fluorophenyl	391
2,4-difluorophenyl	phenyl	325	2,6-diisopropylphenyl	2,4-difluorophenyl	409
2,4-difluorophenyl	o-tolyl	339	2,6-diisopropylphenyl	2-methoxyphenyl	403
2,4-difluorophenyl	4-chloro-2-methylphenyl	374	2,6-diisopropylphenyl	3-methoxyphenyl	403
2,4-difluorophenyl	2-fluorophenyl	343	2,6-diisopropylphenyl	4-methoxyphenyl	403
2,4-difluorophenyl	3-fluorophenyl	343	2,6-diisopropylphenyl	2,4-dimethoxyphenyl	434
2,4-difluorophenyl	4-fluorophenyl	343	2,6-diisopropylphenyl	2-phenoxyphenyl	466

2, 6-diisopropylphenyl	3-phenoxyphenyl	466
2, 6-diisopropylphenyl	4-phenoxyphenyl	466
2, 6-diisopropylphenyl	4-biphenyl	450
2, 6-diisopropylphenyl	4-benzylphenyl	464
2, 6-diisopropylphenyl	4-(trifluoromethoxy)phenyl	457
2, 6-diisopropylphenyl	cyclohexyl	380
2, 6-diisopropylphenyl	2-methylcyclohexyl	394
2, 6-diisopropylphenyl	cycloheptyl	394
2, 6-diisopropylphenyl	indan-1-yl	414
2, 6-diisopropylphenyl	2-dicyclohexyl	462
2, 4-dimethoxyphenyl	phenyl	349
2, 4-dimethoxyphenyl	o-tolyl	363
2, 4-dimethoxyphenyl	4-chloro-2-methylphenyl	398
2, 4-dimethoxyphenyl	2-fluorophenyl	367
2, 4-dimethoxyphenyl	3-fluorophenyl	367
2, 4-dimethoxyphenyl	4-fluorophenyl	367
2, 4-dimethoxyphenyl	2, 4-difluorophenyl	385
2, 4-dimethoxyphenyl	2-methoxyphenyl	379
2, 4-dimethoxyphenyl	3-methoxyphenyl	379
2, 4-dimethoxyphenyl	4-methoxyphenyl	379
2, 4-dimethoxyphenyl	2, 4-dimethoxyphenyl	409
2, 4-dimethoxyphenyl	2-phenoxyphenyl	441
2, 4-dimethoxyphenyl	3-phenoxyphenyl	441
2, 4-dimethoxyphenyl	4-phenoxyphenyl	441
2, 4-dimethoxyphenyl	4-biphenyl	425
2, 4-dimethoxyphenyl	4-benzylphenyl	439
2, 4-dimethoxyphenyl	4-(trifluoromethoxy)phenyl	433
2, 4-dimethoxyphenyl	3-trifluoromethylphenyl	417

2, 4-dimethoxyphenyl	cyclohexyl	355
2, 4-dimethoxyphenyl	2-methylcyclohexyl	369
3-methoxyphenyl	phenyl	319
3-methoxyphenyl	o-tolyl	333
3-methoxyphenyl	4-chloro-2-methylphenyl	368
3-methoxyphenyl	2-fluorophenyl	337
3-methoxyphenyl	3-fluorophenyl	337
3-methoxyphenyl	4-fluorophenyl	337
3-methoxyphenyl	2, 4-difluorophenyl	355
3-methoxyphenyl	2-methoxyphenyl	349
3-methoxyphenyl	3-methoxyphenyl	349
3-methoxyphenyl	4-methoxyphenyl	349
3-methoxyphenyl	2, 4-dimethoxyphenyl	379
3-methoxyphenyl	2-phenoxyphenyl	411
3-methoxyphenyl	3-phenoxyphenyl	411
3-methoxyphenyl	4-phenoxyphenyl	411
3-methoxyphenyl	4-biphenyl	395
3-methoxyphenyl	4-benzylphenyl	409
3-methoxyphenyl	4-(trifluoromethoxy)phenyl	403
3-methoxyphenyl	3-trifluoromethylphenyl	387
3-methoxyphenyl	cyclohexyl	625
3-methoxyphenyl	2-methylcyclohexyl	339
4-methoxyphenyl	phenyl	319
4-methoxyphenyl	o-tolyl	333
4-methoxyphenyl	4-chloro-2-methylphenyl	368
4-methoxyphenyl	2-fluorophenyl	337
4-methoxyphenyl	3-fluorophenyl	337
4-methoxyphenyl	4-fluorophenyl	337

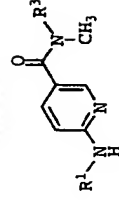
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4-methoxyphenyl	2,4-difluorophenyl	355
4-methoxyphenyl	2-methoxyphenyl	349
4-methoxyphenyl	3-methoxyphenyl	349
4-methoxyphenyl	4-methoxyphenyl	349
4-methoxyphenyl	2,4-dimethoxyphenyl	379
4-methoxyphenyl	2-phenoxyphenyl	411
4-methoxyphenyl	3-phenoxyphenyl	411
4-methoxyphenyl	4-phenoxyphenyl	411
4-methoxyphenyl	4-biphenyl	395
4-methoxyphenyl	4-benzylphenyl	409
4-methoxyphenyl	4-(trifluoromethoxy)phenyl	403
4-methoxyphenyl	3-trifluoromethylphenyl	387
4-methoxyphenyl	cyclohexyl	625
4-methoxyphenyl	2-methylcyclohexyl	339
4-methoxyphenyl	phenyl	338
4-methoxyphenyl	o-tolyl	352
4-methoxyphenyl	4-chloro-2-methylphenyl	386
4-methoxyphenyl	2-fluorophenyl	356
4-methoxyphenyl	3-fluorophenyl	356
4-methoxyphenyl	4-fluorophenyl	356
4-methoxyphenyl	2,4-difluorophenyl	374
4-methoxyphenyl	2-methoxyphenyl	368
4-methoxyphenyl	3-methoxyphenyl	368
4-methoxyphenyl	4-methoxyphenyl	368
4-methoxyphenyl	2,4-dimethoxyphenyl	398
4-methoxyphenyl	2-phenoxyphenyl	430
4-methoxyphenyl	3-phenoxyphenyl	430
4-methoxyphenyl	4-phenoxyphenyl	430
4-methoxyphenyl	4-biphenyl	414

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2-methoxyphenyl	4-biphenyl	395
2-methoxyphenyl	4-benzylphenyl	409
2-methoxyphenyl	4-(trifluoromethoxy)phenyl	403
2-methoxyphenyl	3-trifluoromethylphenyl	387
2-methoxyphenyl	cyclohexyl	625
2-methoxyphenyl	2-methylcyclohexyl	339

Table 9

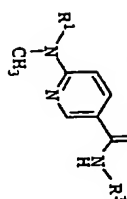


R ¹	R ³	MS (m/z)
4-chlorophenyl	phenyl	338
4-chlorophenyl	o-tolyl	352
4-chlorophenyl	4-chloro-2-methylphenyl	386
4-chlorophenyl	2-fluorophenyl	356
4-chlorophenyl	3-fluorophenyl	356
4-chlorophenyl	4-fluorophenyl	356
4-chlorophenyl	2,4-difluorophenyl	374
4-chlorophenyl	2-methoxyphenyl	368
4-chlorophenyl	3-methoxyphenyl	368
4-chlorophenyl	4-methoxyphenyl	368
4-chlorophenyl	2,4-dimethoxyphenyl	398
4-chlorophenyl	2-phenoxyphenyl	430
4-chlorophenyl	3-phenoxyphenyl	430
4-chlorophenyl	4-phenoxyphenyl	430
4-chlorophenyl	4-biphenyl	414

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200

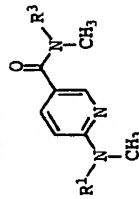
Table 10



4-chlorophenyl	4-benzylphenyl	428	o-tolyl	N-methylphenyl	317
4-chlorophenyl	4-(trifluoromethoxy)phenyl	422	o-tolyl	4-chloro-N-methylphenyl	352
4-chlorophenyl	cyclohexyl	344	2-fluorophenyl	N-methylcyclohexyl	323
4-chlorophenyl	2-methylcyclohexyl	358	2-fluorophenyl	N-methylphenyl	321
phenyl	phenyl	303	2-fluorophenyl	4-chloro-N-methylphenyl	356
phenyl	o-tolyl	317	2-fluorophenyl	N-methylcyclohexyl	327
phenyl	4-chloro-2-methylphenyl	352	2-fluorophenyl	N-methylphenyl	331
phenyl	2-fluorophenyl	321	2-fluorophenyl	4-chloro-N-methylphenyl	366
phenyl	3-fluorophenyl	321	2-fluorophenyl	N-methylcyclohexyl	337
phenyl	4-fluorophenyl	321	2-fluorophenyl	N-methylphenyl	395
phenyl	2,4-difluorophenyl	339	2-fluorophenyl	4-chloro-N-methylphenyl	430
phenyl	2-methoxyphenyl	333	2-fluorophenyl	N-methylcyclohexyl	401
phenyl	3-methoxyphenyl	333	2-fluorophenyl	N-methylphenyl	303
phenyl	4-methoxyphenyl	333	2-fluorophenyl	4-chloro-N-methylphenyl	338
phenyl	2,4-dimethoxyphenyl	363	2-fluorophenyl	N-methylcyclohexyl	309
phenyl	2-phenoxyphenyl	395	2-fluorophenyl	N-methylphenyl	339
phenyl	3-phenoxyphenyl	395	2-fluorophenyl	4-chloro-N-methylphenyl	374
phenyl	4-phenoxyphenyl	395	2-fluorophenyl	N-methylcyclohexyl	345
phenyl	4-biphenyl	379	2-fluorophenyl	N-methylphenyl	387
phenyl	4-benzylphenyl	393	2-fluorophenyl	4-chloro-N-methylphenyl	309
phenyl	4-(trifluoromethoxy)phenyl	387	2-fluorophenyl	N-methylcyclohexyl	339
phenyl	3-trifluoromethylphenyl	371	2-fluorophenyl	N-methylphenyl	374
phenyl	cyclohexyl	309	2-fluorophenyl	4-chloro-N-methylphenyl	422
phenyl	2-methylcyclohexyl	323	2-fluorophenyl	N-methylcyclohexyl	394

2, 4-dimethoxyphenyl	N-methylphenyl	363
2, 4-dimethoxyphenyl	4-chloro-N-methylphenyl	398
2, 4-dimethoxyphenyl	N-methylcyclohexyl	369
3-methoxyphenyl	N-methylphenyl	333
3-methoxyphenyl	4-chloro-N-methylphenyl	368
3-methoxyphenyl	N-methylcyclohexyl	339
4-methoxyphenyl	N-methylphenyl	333
4-methoxyphenyl	4-chloro-N-methylphenyl	368
4-methoxyphenyl	N-methylcyclohexyl	339
2-methoxyphenyl	N-methylphenyl	333
2-methoxyphenyl	4-chloro-N-methylphenyl	368
2-methoxyphenyl	N-methylcyclohexyl	339

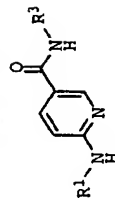
Table 11



R ¹	R ³	MS (m/z)
4-chlorophenyl	phenyl	352
4-chlorophenyl	4-chlorophenyl	386
4-chlorophenyl	cyclohexyl	358
phenyl	phenyl	317
phenyl	4-chlorophenyl	352
phenyl	cyclohexyl	323

compounds and the appropriate amine according to the general procedure above.

Table 12

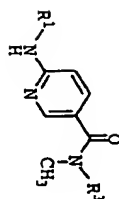


R ¹	R ³
o-tolyl	3-trifluoromethylphenyl
2-fluorophenyl	3-trifluoromethylphenyl
2, 6-dimethylphenyl	3-trifluoromethylphenyl
2-phenoxyphenyl	3-trifluoromethylphenyl
phenyl	3-trifluoromethylphenyl
2, 4-difluorophenyl	3-trifluoromethylphenyl
2, 6-diisopropylphenyl	3-trifluoromethylphenyl
2, 4-dimethoxyphenyl	cycloheptyl
2, 4-dimethoxyphenyl	indan-1-yl
2, 4-dimethoxyphenyl	2-dicyclohexyl
3-methoxyphenyl	cycloheptyl
3-methoxyphenyl	indan-1-yl
3-methoxyphenyl	2-dicyclohexyl
4-methoxyphenyl	cycloheptyl
4-methoxyphenyl	indan-1-yl
4-methoxyphenyl	2-dicyclohexyl
2-methoxyphenyl	cycloheptyl
2-methoxyphenyl	indan-1-yl
2-methoxyphenyl	2-dicyclohexyl

The compounds listed in Tables 12-13 can be prepared from 6-chloro-N-substituted nicotinamides

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Table 11



R ¹	R ²
4-chlorophenyl	3-trifluoromethylphenyl
4-chlorophenyl	cycloheptyl
4-chlorophenyl	indan-1-yl
4-chlorophenyl	2-dicyclohexyl
phenyl	cycloheptyl
phenyl	indan-1-yl
phenyl	2-dicyclohexyl

Example 20

The following assays were used to characterize the ability of compounds of the invention to inhibit the production of TNF- α and IL-1 β . The second assay measured the inhibition of TNF- α and/or IL-1 β in mice after oral administration of the test compounds. The third assay, a glucagon binding inhibition in vitro assay, can be used to characterize the ability of compounds of the invention to inhibit glucagon binding. The fourth assay, a Cyclooxygenase enzyme (COX-1 and COX-2) inhibition activity in vitro assay, can be used to characterize the ability of compounds of the invention to inhibit COX-1 and/or COX-2. The fifth assay, a Raf-kinase inhibition assay, can be used to characterize the compounds of the invention to inhibit phosphorylation of MEK by activated Raf-kinase.

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Lipopolysaccharide-activated monocyte TNF production assay

Isolation of monocytes

Test compounds were evaluated in vitro for the ability to inhibit the production of tumor necrosis factor (TNF) by monocytes activated with bacterial lipopolysaccharide (LPS). Fresh residual source leukocytes (a byproduct of plateletpheresis) were obtained from a local blood bank, and peripheral blood mononuclear cells (PBMCs) were isolated by density gradient centrifugation on Ficoll-Paque Plus (Pharmacia). PBMCs were suspended at 2×10^6 /ml in DMEM supplemented to contain 2% FCS, 10 mM, 0.3 mg/ml glutamate, 100 U/ml penicillin G and 100 mg/ml streptomycin sulfate (complete media). Cells were plated into Falcon flat bottom, 96 well culture plates (200 μ l/well) and cultured overnight at 37°C and 6% CO₂. Non-adherent cells were removed by washing with 200 μ l/well of fresh medium. Wells containing adherent cells ($\sim 70\%$ monocytes) were replenished with 100 μ l of fresh medium.

Preparation of test compound stock solutions

Test compounds were dissolved in DMSO. Compound stock solutions were prepared to an initial concentration of 10 - 50 μ M. Stocks were diluted initially to 20 - 200 μ M in complete media. Nine two-fold serial dilutions of each compound were then prepared in complete medium.

Treatment of cells with test compounds and activation of TNF production with lipopolysaccharide

One hundred microliters of each test compound dilution were added to microtiter wells containing adherent monocytes and 100 μ l complete medium. Monocytes were cultured with test compounds for 60 min at which time 25 μ l of complete medium containing 30

ng/ml lipopolysaccharide from *E. coli* K532 were added to each well. Cells were cultured an additional 4 hrs. Culture supernatants were then removed and TNF presence in the supernatants was quantified using an ELISA.

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TNF ELISA

Flat bottom, 96 well Corning High Binding ELISA plates were coated overnight (4°C) with 150 µL/well of 3 µg/ml murine anti-human TNF-α MAb (R&D Systems #MAB210). Wells were then blocked for 1 hr at room temperature with 200 µL/well of CaCl₂-free ELISA buffer supplemented to contain 20 mg/ml BSA (standard ELISA buffer: 20 mM, 150 mM NaCl, 2 mM CaCl₂, 0.15 mM thimerosal, pH 7.4). Plates were washed and replenished with 100 µl of test supernatants (diluted 1:3) or standards. Standards consisted of eleven 1.5-fold serial dilutions from a stock of 1 ng/ml recombinant human TNF (R&D Systems). Plates were incubated at room temperature for 1 hr on orbital shaker (300 rpm), washed and replenished with 100 µl/well of 0.5 µg/ml goat anti-human TNF-α (R&D systems #AB-210-NA) biotinylated at a 4:1 ratio. Plates were incubated for 40 min, washed and replenished with 100 µl/well of alkaline phosphatase-conjugated streptavidin (Jackson ImmunoResearch #016-050-084) at 0.02 µg/ml. Plates were incubated 30 min, washed and replenished with 200 µl/well of 1 mg/ml of p-nitrophenyl phosphate. After 30 min, plates were read at 405 nm on a V_{max} plate reader.

30 Data analysis

Standard curve data were fit to a second order polynomial and unknown TNF-α concentrations determined from their OD by solving this equation for concentration. TNF concentrations were then plotted vs. test compound concentration using a second order polynomial. This equation was then used to calculate

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the concentration of test compounds causing a 50% reduction in TNF production.

The following compounds had an IC₅₀ of less than 15 µM:

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2-cyclohexyloxy-5-(2-chlorophenylcarbonylamino)pyridine;
2-cyclohexyloxy-5-(2-methylphenylcarbonylamino)pyridine;
2-cyclohexyloxy-5-(2,6-dichlorophenylcarbonylamino)pyridine;

10 2-cyclohexyloxy-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2,4-dimethylphenoxy)-5-(2-methylphenylcarbonylamino)pyridine;

15 2-(2-methyl-4-fluorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2-chlorophenylcarbonylamino)pyridine;

2-(2-methyl-4-chlorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;

20 2-(2-methyl-4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;

2-(2-methyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;

25 2-(2-methyl-4-fluorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;

2-(2-methyl-4-fluorophenoxy)-5-(2-fluorophenylcarbonylamino)pyridine;

30 2-(2,4-dimethylphenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;

2-(1-naphthyl-4-fluorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;

35 2-(1-naphthyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;

2-(2-methyl-3-pyridyloxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;

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- 2-(2-methyl-4-chlorophenoxy)-5-((3,5-dimethyl-4-isoxazolyl)carbonylamino)pyridine;
2-cyclohexylamino-5-(2,6-dichlorophenylcarbonylamino)pyridine;
2-cyclohexylamino-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2-methylcyclohexylamino)-5-(2,6-dichlorophenylcarbonyl amino)pyridine;
2-(2-methylcyclohexylamino)-5-(2-methylphenylcarbonyl amino)pyridine;
2-(2-methylphenylamino)-5-(2-methylphenylcarbonyl amino)pyridine;
2-(2-methylphenylamino)-5-(2,6-dimethylphenylcarbonyl amino)pyridine;
2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenylcarbonylamino)pyridine; and
2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenylaminocarbonyl)pyridine.

Compounds of the invention can also be shown to inhibit LPS-induced release of IL-1 β , IL-6 and/or IL-8 from monocytes by measuring concentrations of IL-1 β , IL-6 and/or IL-8 by methods well known to those skilled in the art. In a similar manner to the above described assay involving the LPS induced release of TNF- α from monocytes, compounds of this invention can also be shown to inhibit LPS induced release of IL-1 β , IL-6 and/or IL-8 from monocytes by measuring concentrations of IL-1 β , IL-6 and/or IL-8 by methods well known to those skilled in the art. Thus, the compounds of the invention may lower elevated levels of TNF- α , IL-1, IL-6, and IL-8 levels. Reducing elevated levels of these inflammatory cytokines to basal levels or below is favorable in controlling, slowing progression, and alleviating many disease states. All of the compounds are useful in the methods of treating disease states in which TNF- α , IL-

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1 β , IL-6, and IL-8 play a role to the full extent of the definition of TNF- α -mediated diseases described herein.

Inhibition of LPS-Induced TNF- α production in mice

Male DBA/1JACJ mice are dosed with vehicle or test compounds in a vehicle (the vehicle consisting of 0.5% treagacanth in 0.03 N HCl) 30 minutes prior to lipopolysaccharide (2 mg/kg, I.V.) injection. Ninety minutes after LPS injection, blood are collected and the serum is analyzed by ELISA for TNF levels.

Selected compounds from the class have shown in vivo activity in a LPS mouse model in which serum levels of TNF- α were reduced in the presence of compounds of this invention.

Compounds of the invention may be shown to have anti-inflammatory properties in animal models of inflammation, including carageenan paw edema, collagen induced arthritis and adjuvant arthritis, such as the carageenan paw edema model (C. A. Winter et al Proc. Soc. Exp. Biol. Med. (1962) vol 111, p 544; K. F. Swingle, in R. A. Scherrer and M. W. Whitehouse, Eds., Antinflammatory Agents, Chemistry and Pharmacology, Vol. 13-II, Academic, New York, 1974, p. 33) and collagen induced arthritis (D. E. Trentham et al J. Exp. Med. (1977) vol. 146, p 857; J. S. Courtenay, Nature (New Biol.) (1980), Vol 283, p 666).

¹²⁵I-Glucagon Binding Screen with CHO/hgR cells

The assay is described in WO 97/16442, which is incorporated herein by reference in its entirety.

Reagents

The reagents can be prepared as follows: (a) prepare fresh 1M o-Phenanthroline (Aldrich) (198.2 mg/ml ethanol); (b) prepare fresh 0.5M DTT (Sigma); (c) Protease Inhibitor Mix (1000X): 5 mg leupeptin, 10 mg

benzamidine, 40 mg bacitracin and 5 mg soybean trypsin inhibitor per ml DMSO and store aliquots at -20°C; (d) 250 μ M human glucagon (Peninsula); solubilize 0.5 mg vial in 575 μ l 0.1N acetic acid (1 μ l yields 1 μ M final concentration in assay for non-specific binding) and store in aliquots at -20°C; (e) Assay Buffer: 20mM Tris (pH 7.8), 1 mM DTT and 3 mM o-phenanthroline; (f) Assay Buffer with 0.1% BSA (for dilution of label only; 0.01% final in assay); 10 μ l 10% BSA (heat-inactivated) and 990 μ l Assay Buffer; (g) 125 I-Glucagon (NEN, receptor-grade, 2200 Ci/mmol): dilute to 50,000 cpm/25 μ l in assay buffer with BSA (about 50pM final concentration in assay).

15 Harvesting of CHO/hGLUR Cells for Assay

1. Remove media from confluent flask then rinse once each with PBS (Ca, Mg-free) and Enzyme-free Dissociation Fluid (Specialty Media, Inc.).
2. Add 10 ml Enzyme-free Dissoc. Fluid and hold for about 4 min. at 37°C.
3. Gently tap cells free, triturate, take aliquot for counting and centrifuge remainder for 5 min. at 1000 rpm.
4. Resuspend pellet in Assay Buffer at 75000 cells per 100 μ l.

Membrane preparations of CHO/hGLUR cells can be used in place of whole cells at the same assay volume. Final protein concentration of a membrane preparation is determined on a per batch basis.

30 Assay

The determination of inhibition of glucagon binding can be carried out by measuring the reduction of I^{125} -

- glucagon binding in the presence of compounds of Formula I. The reagents are combined in 120 μ l of assay buffer as follows:

	Compound/ Vehicle	250 μ M Glucagon	125 I- Glucagon	CHO/hGLUR Cells
Total	--/5 μ l	--	25 μ l	100 μ l
Binding				
+	5 μ l/--	--	25 μ l	100 μ l
Compound				
Nonspecific	--/5 μ l	1 μ l	25 μ l	100 μ l
ic				
Binding				

The mixture is incubated for 60 min. at 22°C on a shaker at 275 rpm. The mixture is filtered over pre-soaked (0.5% polyethylimine (PEI)) GF/C filtermat using an Innotech Harvester or Tomtec Harvester with four washes of ice-cold 20mM Tris buffer (pH 7.8). The radioactivity in the filters is determined by a gamma-scintillation counter.

- Thus, compounds of the invention may also be shown to inhibit the binding of glucagon to glucagon receptors.

Cyclooxygenase Enzyme Activity Assay

- The human monocytic leukemia cell line, THP-1, differentiated by exposure to phorbol esters expresses only COX-1; the human osteosarcoma cell line 143B expresses predominantly COX-2. THP-1 cells are routinely cultured in RPMI complete media supplemented with 10% FBS and human osteosarcoma cells (HOSC) are cultured in minimal essential media supplemented with 10% fetal bovine serum (MEM-10%FBS); all cell incubations are at 37°C in a humidified environment containing 5% CO₂.

COX-1 Assay

In preparation for the COX-1 assay, THP-1 cells are grown to confluency, split 1:3 into RPMI containing 2%

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FBS and 10 mM phorbol 12-myristate 13-acetate (TPA), and incubated for 48 hours on a shaker to prevent attachment. Cells are pelleted and resuspended in Hank's Buffered Saline (HBS) at a concentration of 2.5×10^6 cells/mL and plated in 96-well culture plates at a density of 5×10^5 cells/mL. Test compounds are diluted in HBS and added to the desired final concentration and the cells are incubated for an additional 4 hours. Arachidonic acid is added to a final concentration of 30 mM, the cells incubated for 20 minutes at 37°C, and enzyme activity determined as described below.

COX-2 Assay

For the COX-2 assay, subconfluent HOSC are trypsinized and resuspended at 3×10^6 cells/mL in MEM-FBS containing 1 ng human IL-1b/mL, plated in 96-well tissue culture plates at a density of 3×10^5 cells per well, incubated on a shaker for 1 hour to evenly distribute cells, followed by an additional 2 hour static incubation to allow attachment. The media is then replaced with MEM containing 2% FBS (MEM-2%FBS) and 1 ng human IL-1b/mL, and the cells incubated for 18-22 hours. Following replacement of media with 190 mL MEM, 10 mL of test compound diluted in HBS is added to achieve the desired concentration and the cells incubated for 4 hours. The supernatants are removed and replaced with MEM containing 30 mM arachidonic acid, the cells incubated for 20 minutes at 37°C, and enzyme activity determined as described below.

COX Activity Determined

After incubation with arachidonic acid, the reactions are stopped by the addition of 1 N HCl, followed by neutralization with 1 N NaOH and centrifugation to pellet cell debris. Cyclooxygenase enzyme activity in both HOSC and THP-1 cell supernatants

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is determined by measuring the concentration of PGE₂ using a commercially available ELISA (Neogen #404110). A standard curve of PGE₂ is used for calibration, and commercially available COX-1 and COX-2 inhibitors are included as standard controls.

The following compound exhibits activities in the Cyclooxygenase assay with IC₅₀ values of 10 μM or less: 2-(2,4-dimethylphenylamino)-5-(12,6-dichlorophenylcarbonyl)amino)pyridine.

Raf Kinase assay

In vitro Raf kinase activity is measured by the extent of phosphorylation of the substrate MEK (Map kinase/ERK kinase) by activated Raf kinase. Phosphorylated MEK is trapped on a filter and incorporation of radiolabeled phosphate is quantified by scintillation counting.

MATERIALS:

Activated Raf is produced by triple transfection of Sf9 cells with baculoviruses expressing "Glu-Glu"-epitope tagged Raf, val¹⁹-H-Ras, and Lck. The "Glu-Glu"-epitope, Glu-Tyr-Met-Pro-Met-Glu, was fused to the carboxy-terminus of full length c-Raf. Catalytically inactive MEK (K97A mutation) is produced in Sf9 cells transfected with a baculovirus expressing c-terminus "Glu-Glu" epitope-tagged K97A MEK. Anti "Glu-Glu" antibody was purified from cells grown as described in: Grussemeyer, et al., Proceedings of the National Academy of Science, U.S.A. pp 7952-7954, 1985. Column buffer: 20 mM Tris pH=8, 100 mM NaCl, 1 mM EDTA, 2.5 mM EGTA, 10 mM MgCl₂, 2 mM DTT, 0.4 mM AEBSF, 0.1% n-octylglucopyranoside, 1 mM oxaloic acid, and 10 μg/mL each of benzamide, leupeptin, pepstatin, and aprotinin.

5x Reaction buffer: 125 mM HEPES pH=8, 25 mM MgCl₂, 5 mM EDTA, 5 mM Na₂VO₄, 100 µg/mL BSA.

Enzyme dilution buffer: 25 mM HEPES pH=8, 1 mM EDTA, 1 mM Na₂VO₄, 400 µg/mL BSA.

5 Stop solution: 100 mM EDTA, 80 mM sodium pyrophosphate.

Filter plates: Millipore multiscreen # SE3MO78E3, Immobilon-P (PVDF).

METHODS:

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Protein purification: Sf9 cells were infected with baculovirus and grown as described in Williams, et al., Proceedings of the National Academy of Science, U.S.A. pp 2922-2926, 1992. All subsequent steps were performed

15 on ice or at 4 °C. Cells were pelleted and lysed by sonication in column buffer. Lysates were spun at 17,000xg for 20 min, followed by 0.22 µm filtration.

Epitope tagged proteins were purified by chromatography over GammaBind Plus affinity column to which the "Glu-
20 Glu" antibody was coupled. Proteins were loaded on the column followed by sequential washes with two column volumes of column buffer, and eluted with 50 µg/mL Glu-Tyr-Met-Pro-Met-Glu in column buffer.

25 Raf kinase assay: Test compounds were evaluated using ten 3-fold serial dilutions starting at 10 - 100 µM. 10 µL of the test inhibitor or control, dissolved in 10% DMSO, was added to the assay plate followed by the addition of 30 µL of the a mixture containing 10 µL 5x

30 reaction buffer, 1mM 33P-γ-ATP (20 µCi/mL), 0.5 µL MEK (2.5 mg/mL), 1 µL 50 mM β-mercaptoethanol. The reaction was started by the addition of 10 µL of enzyme dilution buffer containing 1 mM DTT and an amount of activated Raf that produces linear kinetics over the reaction time
35 course. The reaction was mixed and incubated at room

temperature for 90 min. and stopped by the addition of 50 µL stop solution. 90 µL aliquots of this stopped solution were transferred onto GFP-30 cellulose microtiter filter plates (Polyfilterics), the filter
5 plates washed in four well volumes of 5% phosphoric acid, allowed to dry, and then replenished with 25 µL scintillation cocktail. The plates were counted for 33p gamma emission using a TopCount Scintillation Reader.

Accordingly, the compounds of the invention or a pharmaceutical composition thereof are useful for
10 prophylaxis and treatment of rheumatoid arthritis; Pagets disease; osteoporosis; multiple myeloma; uveitis; acute and chronic myelogenous leukemia; pancreatic & cell destruction; osteoarthritis;
15 rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; muscle degeneration; cachexia; Reiter's
20 syndrome; type I and type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; stroke; myocardial infarction; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic
25 shock syndrome; fever, and myalgias due to infection. HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses (including HSV-1, HSV-2), and herpes zoster, all of which are sensitive to TNF-α and/or IL-1 inhibition or glucagon antagonism, will also
30 be positively effected by the compounds and methods of the invention.

The compounds of the present invention may also possess oncolytic characteristics and may be useful for the treatment of cancer. The compounds of the present
35 invention may also block signal transduction by extracellular mitogenic stimuli and oncoproteins through inhibition of Raf kinase.

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The compounds of the present invention also may possess analgesic properties and may be useful for the treatment of pain disorders, such as hyperalgesia due to excessive IL-1. The compounds of the present invention may also prevent the production of prostaglandins by inhibition of enzymes in the human arachidonic acid/prostaglandin pathway, including cyclooxygenase (WO 96/03387, incorporated herein by reference in its entirety).

10 Because of their ability to lower TNF- α and IL-1 concentrations or inhibit glucagon binding to its receptor, the compounds of the invention are also useful research tools for studying the physiology associated with blocking these effects.

15 The methods of the invention comprise administering an effective dose of a compound of the invention, a pharmaceutical salt thereof, or a pharmaceutical composition of either, to a subject (i.e., an animal, preferably a mammal, most preferably a human) in need of a reduction in the level of TNF- α , IL-1, IL-6, and/or IL-8 levels and/or reduction in plasma glucose levels and/or which subject may be suffering from rheumatoid arthritis; Pagets disease; osteoporosis; multiple myeloma; uveitis; acute and chronic myelogenous leukemia; pancreatic β cell destruction; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; muscle degeneration; cachexia; Reiter's syndrome; type I and type II diabetes; cancer; bone resorption diseases; graft vs. host reaction; Alzheimer's disease; stroke; myocardial infarction; ischemia reperfusion injury; atherosclerosis; brain trauma; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever, and myalgias due to infection, or which subject is infected by HIV-1.

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HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses (including HSV-1, HSV-2), or herpes zoster.

5 In another aspect, this invention comprises the use of a compound of the invention, or pharmaceutically acceptable salts thereof, in the manufacture of a medicament for the treatment either acutely or chronically of a TNF- α , IL-1 β , IL-6, and/or IL-8 mediated disease state, including those described previously. The compounds of the present are also useful in the manufacture of an anti-cancer medicament. The compounds of the present invention are also useful in the manufacture of a medicament to attenuate or prevent signal transduction by extracellular mitogenic stimuli and oncoproteins through inhibition of Raf kinase.

10 Also, the compounds of this invention are useful in the manufacture of an analgesic medicament and a medicament for treating pain disorders, such as hyperalgesia. The compounds of the present invention also are useful in the manufacture of a medicament to prevent the production of prostaglandins by inhibition of enzymes in the human arachidonic acid/prostaglandin pathway.

15 In still another aspect, this invention provides a pharmaceutical composition comprising an effective TNF- α , IL-1 β , IL-6, and/or IL-8 lowering amount and/or effective plasma glucose level lowering amount, and/or effective tumor suppressing amount of a compound of the invention and a pharmaceutically acceptable carrier or diluent, and if desired other active ingredients. The compounds of the invention are administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended.

20 Therapeutically effective doses of the compounds of the present invention required to arrest the progress or prevent tissue damage associated with the disease are

readily ascertained by one of ordinary skill in the art using standard methods.

For the treatment of TNF- α , IL-1 β , IL-6, and IL-8 mediated diseases, cancer, and/or hyperglycemia, the compounds of the present invention may be administered orally, parentally, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants, and vehicles. The term parenteral as used herein includes, subcutaneous, intravenous, intramuscular, intrasternal, infusion techniques or intraperitoneally.

The dosage regimen for treating a TNF- α , IL-1, IL-6, and IL-8 mediated diseases, cancer, and/or hyperglycemia with the compounds of this invention and/or compositions of this invention is based on a variety of factors, including the type of disease, the age, weight, sex, medical condition of the patient, the severity of the condition, the route of administration, and the particular compound employed. Thus, the dosage regimen may vary widely, but can be determined routinely using standard methods. Dosage levels of the order from about 0.01 mg to 30 mg per kilogram of body weight per day, preferably from about 0.1 mg to 10 mg/kg, more preferably from about 0.25 mg to 1 mg/kg are useful for all methods of use disclosed herein.

The pharmaceutically active compounds of this invention can be processed in accordance with conventional methods of pharmacy to produce medicinal agents for administration to patients, including humans and other mammals.

For oral administration, the pharmaceutical composition may be in the form of, for example, a capsule, a tablet, a suspension, or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a given amount of the active ingredient. For example, these may contain an

amount of active ingredient from about 1 to 2000 mg, preferably from about 1 to 500 mg, more preferably from about 5 to 150 mg. A suitable daily dose for a human or other mammal may vary widely depending on the condition of the patient and other factors, but, once again, can be determined using routine methods.

The active ingredient may also be administered by injection as a composition with suitable carriers including saline, dextrose, or water. The daily parenteral dosage regimen will be from about 0.1 to about 30 mg/kg of total body weight, preferably from about 0.1 to about 10 mg/kg, and more preferably from about 0.25 mg to 1 mg/kg.

Injectable preparations, such as sterile injectable aqueous or oleaginous suspensions, may be formulated according to the known are using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed, including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Suppositories for rectal administration of the drug can be prepared by mixing the drug with a suitable non-irritating excipient such as cocoa butter and polyethylene glycols that are solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum and release the drug.

A suitable topical dose of active ingredient of a compound of the invention is 0.1 mg to 150 mg

administered one to four, preferably one or two times daily. For topical administration, the active ingredient may comprise from 0.001% to 10% w/w, e.g., from 1% to 2% by weight of the formulation, although it may comprise as much as 10% w/w, but preferably not more than 5% w/w, and more preferably from 0.1% to 1% of the formulation.

Formulations suitable for topical administration include liquid or semi-liquid preparations suitable for penetration through the skin (e.g., liniments, lotions, ointments, creams, or pastes) and drops suitable for administration to the eye, ear, or nose.

For administration, the compounds of this invention are ordinarily combined with one or more adjuvants appropriate for the indicated route of administration.

The compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanolic acids, stearic acid, talc, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulphuric acids, acacia, gelatin, sodium alginate, and polyvinylpyrrolidone, and/or polyvinyl alcohol, and tableted or encapsulated for conventional

administration. Alternatively, the compounds of this invention may be dissolved in saline, water,

polyethylene glycol, propylene glycol, ethanol, corn oil, peanut oil, cottonseed oil, sesame oil, tragacanth gum, and/or various buffers. Other adjuvants and modes of administration are well known in the pharmaceutical art. The carrier or diluent may include time delay material, such as glyceryl monostearate or glyceryl distearate alone or with a wax, or other materials well known in the art.

The pharmaceutical compositions may be made up in a solid form (including granules, powders or suppositories) or in a liquid form (e.g., solutions, suspensions, or emulsions). The pharmaceutical compositions may be subjected to conventional

pharmaceutical operations such as sterilization and/or may contain conventional adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers, buffers etc.

Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may also comprise, as in normal practice, additional substances other than inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting, sweetening, flavoring, and perfuming agents.

Compounds of the present invention can possess one or more asymmetric carbon atoms and are thus capable of existing in the form of optical isomers as well as in the form of racemic or non-racemic mixtures thereof.

The optical isomers can be obtained by resolution of the racemic mixtures according to conventional processes, e.g., by formation of diastereoisomeric salts, by treatment with an optically active acid or base.

Examples of appropriate acids are tartaric, diacetyltartaric, dibenzoyltartaric, ditoluoyltartaric, and camphorsulfonic acid and then separation of the mixture of diastereoisomers by crystallization followed by liberation of the optically active bases from these salts. A different process for separation of optical isomers involves the use of a chiral chromatography column optimally chosen to maximize the separation of

the enantiomers. Still another available method involves synthesis of covalent diastereoisomeric molecules by reacting compounds of the invention with an optically pure acid in an activated form or an optically pure isocyanate. The synthesized diastereoisomers can be separated by conventional means such as chromatography, distillation, crystallization or sublimation, and then hydrolyzed to deliver the enantiomerically pure compound. The optically active compounds of the invention can likewise be obtained by using active starting materials. These isomers may be in the form of a free acid, a free base, an ester or a salt.

The compounds of the present invention can be used in the form of salts derived from inorganic or organic acids. The salts include, but are not limited to, the following: acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, cyclopentanepropionate, dodecylsulfate, ethanesulfonate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate, lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmoate, pectinate, persulfate, 2-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, mesylate, and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids that may be employed to from pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, sulphuric acid and phosphoric acid and such organic acids as oxalic acid, maleic acid, succinic acid and citric acid. Other examples include salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium or magnesium or with organic bases.

While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more compounds of the invention or other agents. When administered as a combination, the therapeutic agents can be formulated as separate compositions that are given at the same time or different times, or the therapeutic agents can be given as a single composition.

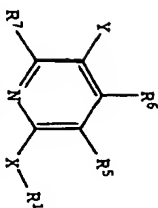
The foregoing is merely illustrative of the invention and is not intended to limit the invention to the disclosed compounds. Variations and changes which are obvious to one skilled in the art are intended to be within the scope and nature of the invention which are defined in the appended claims.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

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WHAT IS CLAIMED IS:

1. A compound of the formula



5 or a pharmaceutically acceptable salt thereof, wherein

X is O, S, S(O), S(O)₂, or NR²;Y is -C(O)-NR³R⁴ or -NR⁴-C(O)-R³;

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R¹ is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of alkyl, halo, haloalkyl, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸ or R¹⁸-Z¹⁸-alkyl; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl

radicals in R¹ is 1-3; and provided when Y is -NR⁴-C(O)-R³ and X is O or S, R¹ is other than a 2-pyrimidinyl radical;

20 R² is a hydrogen or alkyl radical;

25 R³ is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of alkyl, halo, haloalkyl, cyano, azido, nitro, amidino, R¹⁹-Z¹⁹ or R¹⁹-Z¹⁹-alkyl; provided that the total number of aryl and heteroaryl radicals in R³ is 1-3; and provided when Y is -C(O)-NR⁴R³, R³ is other than a phenyl or naphthyl having an amino, nitro, cyano, carboxy or alkoxy carbonyl

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substituent bonded to the ring carbon atom adjacent to the ring carbon atom bonded to -NR⁴-; and

R⁴ is a hydrogen, alkyl, alkenyl, haloalkyl,

5 haloalkenyl, aryl, heteroaryl, arylalkyl,

heteroarylalkyl or R²⁰-Z²⁰-alkyl radical;

wherein R¹⁸, R¹⁹ and R²⁰ are each independently a

10 hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl radical; wherein the aryl and heteroaryl radicals of R⁴, R¹⁸, R¹⁹ and R²⁰ are optionally

substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkylamino, dialkylamino,

alkanoylamino, alkylsulfonylamino, alkylsulfinyl,

15 alkylsulfonyl, alkoxy carbonylamino, alkoxy carbonyl, and cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; and

Z¹⁸, Z¹⁹ and Z²⁰ are each independently -O-, -S-, -S(O)-,

-S(O)₂-, -CO₂-, -C(O)-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-,

20 NR²¹-S(O)₂-, or -S(O)₂-NR²¹-; wherein each R²¹ is

independently a hydrogen or alkyl radical;

30 R⁵ and R⁶ are each independently a hydrogen, alkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, amino, alkylamino, dialkylamino, alkanoylamino, alkylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, hydroxy, hydroxyalkyl, thiol, alkylthiol, alkylsulfinyl, alkylsulfonyl, alkoxy, alkoxyalkyl, cyano, azido, nitro, carboxy, alkoxy carbonyl, aminocarbonyl,

35 alkylaminocarbonyl or dialkylaminocarbonyl radical; and R⁷ is a hydrogen, alkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, hydroxy, hydroxyalkyl, thiol, alkylthiol, alkylsulfinyl, alkylsulfonyl, alkoxy, alkoxyalkyl, cyano, azido, nitro, carboxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl radical.

5

2. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein

10

R^1 is a cycloalkyl, aryl, heterocyclyl or heteroaryl

radical which is optionally substituted by 1-4 radicals of C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl of 1-3 halo

radicals, cyano, azido, nitro, amidino, $R^{18}-Z^{18}$ or R^{18}

$15 \quad Z^{18}-C_1-C_6$ alkyl; provided that the total number of aryl,

heteroaryl, cycloalkyl and heterocyclyl radicals in R^1

is 1-3; and provided when Y is $-NR^4-C(O)-R^3$ and X is O or

S, R^1 is other than a 2-pyrimidinyl radical;

20 R^2 is a hydrogen or C_1-C_4 alkyl radical;

R^3 is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl of 1-3 halo radicals, cyano, azido, nitro,

25 amidino, $R^{19}-Z^{19}$ or $R^{19}-C_1-C_6$ alkyl; provided that the

total number of aryl and heteroaryl radicals in R^3 is 1-

3; and provided when Y is $-C(O)-NR^3R^4$, R^3 is other than a

phenyl or naphthyl having an amino, nitro, cyano,

carboxy or alkoxycarbonyl substituent bonded to the ring

30 carbon atom adjacent to the ring carbon atom bonded to -

NR^4 ; and

R^4 is a radical of hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl of 1-3 halo radicals, C_2-C_6 haloalkenyl of 1-3 halo radicals, aryl, heteroaryl, aryl- C_1-C_4 alkyl, heteroaryl- C_1-C_4 alkyl or $R^{20}-Z^{20}-C_1-C_6$ alkyl 5 radical; and

wherein R^{18} , R^{19} and R^{20} are each independently a

hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl- C_1-C_4 alkyl or

10 heteroaryl- C_1-C_4 alkyl radical; wherein the aryl and

heteroaryl radicals of R^{18} , R^{19} and R^{20} are optionally

substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy,

C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4

alkyl)amino, C_1-C_5 alkanoylamino, C_1-C_4

15 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4

alkylsulfonyl, (C_1-C_4 alkoxy)carbonylamino, (C_1-C_4

alkoxy)carbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4

haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

20

each R^{21} is independently a hydrogen or C_1-C_4 alkyl

radical;

R^5 and R^6 are each independently a hydrogen, C_1-C_4 alkyl,

25 halo, C_1-C_4 haloalkyl of 1-3 halo radicals, C_1-C_4

haloalkoxy of 1-3 halo radicals, C_1-C_4 aminoalkyl, (C_1-C_4

alkyl)amino- C_1-C_4 alkyl, di(C_1-C_4 alkyl)amino- C_1-C_4

alkyl, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, C_1-

C_5 alkanoylamino, C_1-C_4 alkylsulfonylamino,

30 aminosulfonyl, C_1-C_4 alkylaminosulfonyl, di(C_1-C_4

alkyl)aminosulfonyl, hydroxy, C_1-C_4 hydroxyalkyl, thiol,

C_1-C_4 alkylthiol, C_1-C_4 alkylsulfinyl, C_1-C_4

alkylsulfonyl, C_1-C_4 alkoxy, (C_1-C_4 alkoxy) C_1-C_4 alkyl,

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cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

5 R¹ is a hydrogen, C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl of 1-3 halo radicals, C₁-C₄ aminoalkyl, (C₁-C₄ alkyl)amino-C₁-C₄ alkyl, di(C₁-C₄ alkyl)amino-C₁-C₄ alkyl, aminosulfonyl, C₁-C₄ alkylaminosulfonyl, di(C₁-C₄ alkyl)aminosulfonyl, hydroxy, C₁-C₄ hydroxyalkyl, thiol, C₁-C₄ alkylthiol, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, C₁-C₄ alkoxy, (C₁-C₄ alkoxy)C₁-C₄ alkyl, cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

15 wherein cycloalkyl is a monocyclic, bicyclic or tricyclic carbocyclic alkyl radical of 5-12 ring members, which is optionally partially unsaturated, benzo fused or heterocyclo fused; aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclo fused; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; and heteroaryl is a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

35 3. The compound of Claim 2 or a pharmaceutically acceptable salt thereof, wherein Y is -NR¹-C(O)-R².

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4. The compound of Claim 3 or a pharmaceutically acceptable salt thereof, wherein

5 X is O or NR²;

10 R¹ is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of C₁-C₄ alkyl, halo, C₁-C₄ haloalkyl of 1-3 halo radicals, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸- or R¹⁸-Z¹⁸-C₁-C₄ alkyl; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R¹ is 1-2;

15 wherein each R¹⁸ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, acetylamino, cyano, halo, azido, C₁-C₄ alkyl, trifluoromethyl or trifluoromethoxy; and

25 R² is a hydrogen or C₁-C₂ alkyl radical;

R³ is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of C₁-C₆ alkyl, halo, C₁-C₄ haloalkyl of 1-3 halo radicals, cyano, azido, nitro, amidino, R¹⁹-Z¹⁹- or R¹⁹-Z¹⁹-C₁-C₄ alkyl; provided that the total number of aryl and heteroaryl radicals in R³ is 1-2; and

wherein each R^{19} is independently a hydrogen, C_1-C_4 alkyl, trifluoromethyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl or heteroaryl- C_1-C_4 alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, acetylamino, cyano, halo, C_1-C_4 alkyl, trifluoromethyl or trifluoromethoxy; and

10 R^4 is a radical of hydrogen, C_1-C_6 alkyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl, heteroaryl- C_1-C_4 alkyl or $R^{20}-C_2-C_4$ alkyl radical; and

wherein R^{20} is a hydrogen, C_1-C_4 alkyl, aryl, heteroaryl, aryl- C_1-C_2 alkyl or heteroaryl- C_1-C_2 alkyl radical; wherein the aryl and heteroaryl radicals of R^4 and R^{20} are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, acetylamino, halo, C_1-C_4 alkyl, trifluoromethyl or trifluoromethoxy; and

Z^{20} is -O- or -NR²¹-; wherein each R^{21} is independently a hydrogen or methyl radical;

25 R^5 and R^6 are each independently a hydrogen, C_1-C_4 alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, hydroxy, C_1-C_4 hydroxyalkyl, C_1-C_4 alkoxy, cyano, azido, nitro, carboxy, (C_1-C_4 alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

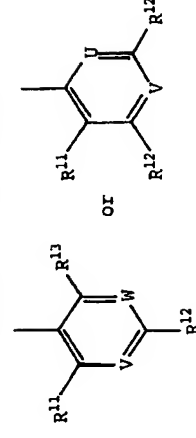
30 (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

R^7 is a hydrogen, C_1-C_4 alkyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, C_1-C_4 hydroxyalkyl, C_1-C_4 alkoxy, carboxy, (C_1-C_4 alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

wherein cycloalkyl is a monocyclic or bicyclic carbocyclic alkyl radical of 5-12 ring members, which is optionally partially unsaturated, benzo fused or heterocyclo fused; aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclo fused; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4 -carbocyclic-fused.

25 5. The compound of Claim 4 or a pharmaceutically acceptable salt thereof, wherein

R^3 is a radical of the formula



30 wherein

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U is C-R¹¹ or N;

V and W are each independently C-R¹² or N;

5 R¹¹ and R¹² are each independently a radical of hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, cyano, azido, nitro, amino or R¹⁹-Z¹⁸; and each R¹² is independently a radical of hydrogen, C₁-C₆ alkyl, halo, C₁-C₄ haloalkyl; 10 of 1-3 halo radicals, R¹¹-Z¹¹ or R¹¹-Z¹¹-C₁-C₄ alkyl; provided that the combined total number of aryl and heteroaryl radicals in R¹¹, R¹² and R¹³ is 0-1;

15 wherein each R¹⁹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, halo, 20 methyl, ethyl, trifluoromethyl or trifluoromethoxy; and each Z¹⁹ is independently -O-, -S(O)₂-, -CO₂-, -C(O)-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂- or -S(O)₂-NR²¹;

25 wherein each R²¹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, 30 methylamino, dimethylamino, acetylamino, cyano, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy; and

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each Z²¹ is independently -O-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂- or -S(O)₂-NR²¹;

5 wherein R⁴ is a radical of hydrogen, C₁-C₆ alkyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl, heteroaryl-C₁-C₄ alkyl or R²⁰-Z²⁰-C₂-C₄ alkyl radical;

10 wherein R²⁰ is a hydrogen, C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical; wherein the aryl and heteroaryl radicals of R⁴ and R²⁰ are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, methylthiol, ethylthiol, amino, methylamino, dimethylamino, ethylamino, diethylamino, acetylamino, halo, methyl, ethyl, trifluoromethyl or 15 trifluoromethoxy; and

20 R⁵ and R⁶ are each independently a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, amino, ethyl, halo, trifluoromethyl, trifluoromethoxy, amino, C₁-C₂ alkylamino, di(C₁-C₂ alkyl)amino, hydroxy, methoxy or ethoxy radical; and

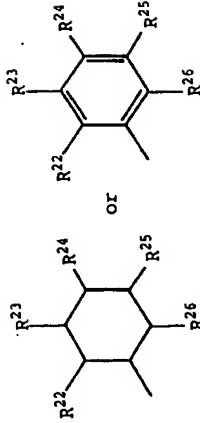
25 R⁷ is a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, methoxy or ethoxy radical; and

30 wherein cycloalkyl is a monocyclic or bicyclic carbocyclic alkyl radical of 5-10 ring members, which is optionally partially unsaturated with one double bond, benzo fused or heterocyclo fused; aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclo fused; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms,

which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

- 10 6. The compound of Claim 5 or a pharmaceutically acceptable salt thereof, wherein

¹ R is a radical of the formula



15 wherein

²² R, ²³ R, ²⁴ R, ²⁵ R and ²⁶ R are each independently a radical of hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸- or R¹⁸-Z¹⁸-C₁-C₄ alkyl; provided at least one of R²¹, R²², R²³, R²⁴ and R²⁵ is hydrogen; and provided that the combined total number of aryl and heteroaryl radicals in R, R²², R²³, R²⁴, R²⁵ and R²⁶ is 0-1;

25 wherein each Z¹⁸ is independently -O-, -S-, -S(O)-, -CO₂-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)-, or -S(O)₂-NR²¹-; and

wherein aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclic fused; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

- 10 7. The compound of Claim 6 or a pharmaceutically acceptable salt thereof, wherein

X is NR²;

15 R² is a hydrogen or methyl radical;

R⁴ is a radical of hydrogen, methyl or ethyl radical; and

20 R⁵, R⁶ and R⁷ are each independently a hydrogen radical; and

wherein aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms.

- 30 8. The compound of Claim 7 or a pharmaceutically acceptable salt thereof, wherein

R¹¹ and R¹³ are each independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, cyano, azido, nitro, amidino, R¹⁹-O-, R¹⁹-S(O)₂-, R¹⁹-O-C(O)-,

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$R^{19}-C(O)-$, $R^{19}-NR^{21}-C(O)-$ or $R^{19}-S(O)_2-$; and each R^{12} is independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, trifluoromethoxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, (methylamino)methyl or (dimethylamino)methyl; provided that the combined total number of aryl and heteroaryl radicals in R^{11} , R^{12} and R^{13} is 0-1; and

10 wherein each R^{19} is independently a hydrogen, methyl, ethyl, trifluoromethyl, phenyl, heteroaryl, phenylmethyl or heteroaryl-methyl radical; wherein the phenyl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, fluoro, chloro, methyl, ethyl, trifluoromethyl or trifluoromethoxy.

20 9. The compound of Claim 2 or a pharmaceutically acceptable salt thereof, wherein Y is $-C(O)-NR^4$.

25 10. The compound of Claim 9 or a pharmaceutically acceptable salt thereof, wherein

X is O or NR^5 ;

30 R^1 is a cycloalkyl, aryl, heterocyclyl or heteroaryl radical which is optionally substituted by 1-4 radicals of C_1-C_4 alkyl, halo, C_1-C_4 haloalkyl of 1-3 halo radicals, cyano, azido, nitro, amidino, $R^{18}-Z^{18}-$ or $R^{18}-Z^{18}-C_1-C_4$ alkyl; provided that the total number of aryl,

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heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 1-2;

5 wherein each R^{18} is independently a hydrogen, C_1-C_4 alkyl, trifluoromethyl, aryl, heteroaryl, aryl- C_1-C_2 alkyl or heteroaryl- C_1-C_2 alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, C_1-C_4 alkylamino, di(C_1-C_4 alkyl)amino, acetylamino, cyano, halo, azido, C_1-C_4 alkyl, trifluoromethyl or trifluoromethoxy; and

10 each Z^{18} is independently -O-, -S-, $-S(O)-$, $-S(O)_2-$, $-CO_2-$, $-C(O)-$, $-NR^{21}-$, $-NR^{21}-C(O)-$, $-C(O)-NR^{21}-$, $-NR^{21}-S(O)_2-$ or $-S(O)_2-NR^{21}-$; wherein each R^{21} is independently a hydrogen or C_1-C_4 alkyl radical;

R^2 is a hydrogen or C_1-C_2 alkyl radical;

20 R^3 is an aryl or heteroaryl radical which is optionally substituted by 1-5 radicals of C_1-C_6 alkyl, halo, C_1-C_4 haloalkyl of 1-3 halo radicals, cyano, azido, nitro, amidino, $R^{19}-Z^{19}-$ or $R^{19}-Z^{19}-C_1-C_4$ alkyl; provided that the total number of aryl and heteroaryl radicals in R^3 is 1-2; and provided R^3 is other than a phenyl or naphthyl having an amino, nitro, cyano, carboxy or alkoxy carbonyl substituent bonded to the ring carbon atom adjacent to the ring carbon atom bonded to $-NR^4$; and

30 wherein each R^{19} is independently a hydrogen, C_1-C_4 alkyl, trifluoromethyl, aryl, heteroaryl, aryl- C_1-C_4 alkyl or heteroaryl- C_1-C_4 alkyl radical; wherein the

aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, acetylamino, cyano, halo, C₁-C₄ alkyl, trifluoromethyl or trifluoromethoxy; and

R⁴ is a radical of hydrogen, C₁-C₆ alkyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl, heteroaryl-C₁-C₄ alkyl or R²⁰-Z²⁰-C₂-C₄ alkyl radical; and

wherein R²⁰ is a hydrogen, C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical;

wherein the aryl and heteroaryl radicals of R⁴ and R²⁰ are optionally substituted by 1-2 radicals of hydroxy, C₁-C₄ alkoxy, C₁-C₄ alkylthiol, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, acetylamino, halo, C₁-C₄ alkyl, trifluoromethyl or trifluoromethoxy; and

Z²⁰ is -O- or -NR²¹-; wherein each R²¹ is independently a hydrogen or methyl radical;

R⁵ and R⁶ are each independently a hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₅ alkanoylamino, hydroxy, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, cyano, azido, nitro, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl, (C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

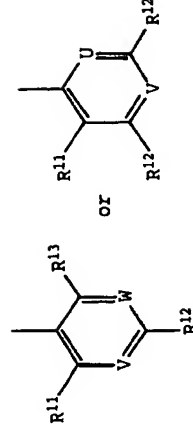
R⁷ is a hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, C₁-C₄ hydroxyalkyl, C₁-C₄ alkoxy, carboxy, (C₁-C₄ alkoxy)carbonyl, aminocarbonyl,

(C₁-C₄ alkyl)aminocarbonyl or di(C₁-C₄ alkyl)aminocarbonyl radical; and

wherein cycloalkyl is a monocyclic or bicyclic carbocyclic alkyl radical of 5-12 ring members, which is optionally partially unsaturated, benzo fused or heterocyclo fused; aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclo fused; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thio radicals; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

11. The compound of Claim 10 or a pharmaceutically acceptable salt thereof, wherein

R³ is a radical of the formula



wherein

U is C-R¹³ or N;

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V and W are each independently C-R¹² or N;

- R¹¹ and R¹³ are each independently a radical of hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, cyano, azido, nitro, amidino or R¹⁹-Z¹⁹; and each R¹² is independently a radical of hydrogen, C₁-C₆ alkyl, halo, C₁-C₄ haloalkyl of 1-3 halo radicals, R¹¹-Z¹¹ or R¹¹-Z¹¹-C₁-C₄ alkyl; provided that the combined total number of aryl and heteroaryl radicals in R¹¹, R¹² and R¹³ is 0-1; provided when U is C-R¹³ and V and W are each C-R¹², R¹¹ and R¹³ are each other than a nitro, cyano, carboxy or alkoxy carbonyl radical;

- wherein each R¹⁹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy; and each Z¹⁹ is independently -O-, -S(O)₂-, -CO₂-, -C(O)-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂-, or -S(O)₂-NR²¹-, wherein each R²¹ is independently a hydrogen or methyl radical;

- wherein each R²¹ is independently a hydrogen, C₁-C₄ alkyl, trifluoromethyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl or heteroaryl-C₁-C₄ alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy; and

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each Z²¹ is independently -O-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)₂-, or -S(O)₂-NR²¹-,

- R⁴ is a radical of hydrogen, C₁-C₆ alkyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl, heteroaryl-C₁-C₄ alkyl or R²⁰-Z²⁰-C₂-C₄ alkyl radical; and wherein R²⁰ is a hydrogen, C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₂ alkyl or heteroaryl-C₁-C₂ alkyl radical; wherein the aryl and heteroaryl radicals of R⁴ and R²⁰ are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, methylthiol, ethylthiol, amino, methylamino, dimethylamino, ethylamino, diethylamino, acetylamino, halo, methyl, ethyl, trifluoromethyl or trifluoromethoxy; and R⁵ and R⁶ are each independently a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, amino, C₁-C₂ alkylamino, di(C₁-C₂ alkyl)amino, hydroxy, methoxy or ethoxy radical; and

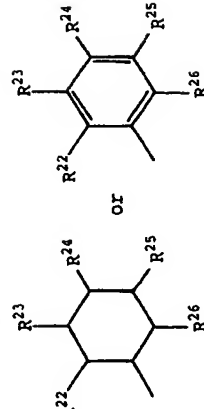
- R⁷ is a hydrogen, methyl, ethyl, halo, trifluoromethyl, trifluoromethoxy, hydroxy, methoxy or ethoxy radical; and wherein cycloalkyl is a monocyclic or bicyclic carbocyclic alkyl radical of 5-10 ring members, which is optionally partially unsaturated with one double bond, benzo fused or heterocyclo fused; aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclo fused; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3

ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

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12. The compound of Claim 11 or a pharmaceutically acceptable salt thereof, wherein

R¹ is a radical of the formula



wherein

R²², R²³, R²⁴, R²⁵ and R²⁶ are each independently a radical of hydrogen, C₁-C₄ alkyl, halo, trifluoromethyl, cyano, azido, nitro, amidino, R¹⁸-Z¹⁸ or R¹⁸-Z¹⁸-C₁-C₄ alkyl; provided at least one of R²¹, R²², R²³, R²⁴ and R²⁵ is hydrogen; and provided that the combined total number of aryl and heteroaryl radicals in R²², R²³, R²⁴, R²⁵ and R²⁶ is 0-1;

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each Z¹⁸ is independently -O-, -S-, -S(O)-, -CO₂-, -NR²¹-, -NR²¹-C(O)-, -C(O)-NR²¹-, -NR²¹-S(O)- or -S(O)-NR²¹-, and

wherein aryl is a phenyl or biphenyl radical which is optionally benzo fused or heterocyclic fused; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C₃-C₄-carbocyclic-fused.

13. The compound of Claim 12 or a pharmaceutically acceptable salt thereof, wherein

X is NR²;

R² is a hydrogen or methyl radical;

R⁴ is a radical of hydrogen, methyl or ethyl radical; and

R⁵, R⁶ and R⁷ are each independently a hydrogen radical; and

wherein aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is a monocyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms.

14. The compound of Claim 13 or a pharmaceutically acceptable salt thereof, wherein

R¹¹ and R¹³ are each independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, cyano, azido, nitro, amidino, R¹⁹-O-, R¹⁹-S(O)₂-, R¹⁹-O-C(O)-,

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R^{18} -C(O)-, R^{19} -NR²¹-C(O)- or R^{19} -S(O)₂-; provided when U is C-R¹³ and V and W are each C-R¹², R¹² and R¹³ are each other than a nitro, cyano, carboxy or alkoxy carbonyl radical; and provided that the combined total number of aryl and heteroaryl radicals in R¹¹ and R¹³ is 0-1;

each R¹² is independently a radical of hydrogen, methyl, ethyl, fluoro, chloro, trifluoromethyl, trifluoromethoxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, methylamino)methyl or (dimethylamino)methyl; and wherein each R¹⁹ is independently a hydrogen, methyl, ethyl, trifluoromethyl, phenyl, heteroaryl, phenylmethyl or heteroaryl-methyl radical; wherein the phenyl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, methoxy, ethoxy, amino, methylamino, dimethylamino, acetylamino, cyano, fluoro, chloro, methyl, ethyl, trifluoromethyl or trifluoromethoxy.

15. The compound of Claim 1 which is:

25 2-cyclohexyloxy-5-(2-chlorophenylcarbonylamino)pyridine;
2-cyclohexyloxy-5-(2-methylphenylcarbonylamino)pyridine;
2-cyclohexyloxy-5-(2,6-dichlorophenylcarbonylamino)pyridine;
30 2-cyclohexyloxy-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2,4-dimethylphenoxy)-5-(2-chlorophenylcarbonylamino)pyridine;
2-(2,4-dimethylphenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
35 amino)pyridine;

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2-(2,4-dimethylphenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(2,6-dimethyl-4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
5 2-(2-methyl-4-fluorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2-chlorophenylcarbonylamino)pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
10 2-(2-methyl-4-chlorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(2-methylphenoxy)-5-(2-chlorophenylcarbonylamino)pyridine;
2-(2-methylphenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
15 2-(2-methylphenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
2-(2-methyl-4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
20 2-(2-methyl-4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(4-chlorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2-methyl-4-fluorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
25 2-(2-methyl-4-fluorophenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2-methylphenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(2-methyl-4-fluorophenoxy)-5-(2-fluorophenylcarbonylamino)pyridine;
30 2-(2,4-dimethylphenoxy)-5-(2,6-dimethylphenylcarbonylamino)pyridine;
2-(1-naphthyl-4-chlorophenoxy)-5-(2-methylphenylcarbonylamino)pyridine;
2-(1-naphthyl-4-chlorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;
35 2-(1-naphthyl-4-chlorophenoxy)-5-(2,6-dichlorophenylcarbonylamino)pyridine;

- 2-(1-naphthyl-3-pyridyl)-5-(2,6-dimethylphenyl)carbonylamino)pyridine;
 2-(2-methyl-3-pyridyl)-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-(2-methyl-4-chlorophenoxy)-5-((3,5-dimethyl-4-isoxazolyl)carbonylamino)pyridine;
 2-(2-methyl-4-chlorophenylthiol)-5-(2-methylphenyl)carbonylamino)pyridine;
 2-(2-methyl-4-chlorophenylthiol)-5-(2,6-dimethylphenyl)carbonylamino)pyridine;
 2-cyclohexylamino-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-cyclohexylamino-5-(2,6-dimethylphenyl)carbonylamino)pyridine;
 2-(2-methylcyclohexylamino)-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-(2-methylcyclohexylamino)-5-(2-methylphenyl)carbonylamino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2-fluorophenyl)carbonylamino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2-chlorophenyl)carbonylamino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-(2-methyl-4-chlorophenylamino)-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-(2-methylphenylamino)-5-(2-methylphenyl)carbonylamino)pyridine;
 2-(2-methylphenylamino)-5-(2,6-dichlorophenyl)carbonylamino)pyridine;
 2-(2-methylphenylamino)-5-(2,6-dimethylphenyl)carbonylamino)pyridine;
 2-(2,4-dimethylphenylamino)-5-(2,6-dimethylphenyl)carbonylamino)pyridine;

- 2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenyl)carbonylamino)pyridine;
 2-(2-methyl-4-chlorophenylamino)-5-(2,6-dimethylphenyl)carbonylamino)pyridine; or
 2-(2-methyl-4-chlorophenylamino)-5-(2-methylphenyl)aminocarbonyl)pyridine.
 16. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.
 17. A method for prophylaxis or treatment of inflammation comprising administering an effective amount of a compound of Claim 1.
 18. A method for prophylaxis or treatment of inflammation comprising administering an effective amount of a composition of Claim 16.
 19. A method of treating cancer which comprises administering an effective amount of a compound of Claim 1.
 20. A method of treating cancer which comprises administering an effective amount of a composition of Claim 16.
 21. A method for prophylaxis or treatment of rheumatoid arthritis, Pagets disease, osteoporosis, multiple myeloma, uveitis, acute or chronic myelogenous leukemia, pancreatic β cell destruction, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome

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(ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, anaphylaxis, contact dermatitis, asthma, muscle degeneration, cachexia, Reiter's syndrome, type I diabetes, type II diabetes, bone resorption diseases, graft vs. host reaction, Alzheimer's disease, stroke, myocardial infarction, ischemia reperfusion injury, atherosclerosis, brain trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock syndrome, fever, myalgias due to HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses or herpes zoster infection in a mammal comprising administering an effective amount of a compound of Claim 1.

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22. A method for prophylaxis or treatment of rheumatoid arthritis, Paget's disease, osteoporosis, multiple myeloma, uveitis, acute or chronic myelogenous leukemia, pancreatic & cell destruction, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, anaphylaxis, contact dermatitis, asthma, muscle degeneration, cachexia, Reiter's syndrome, type I diabetes, type II diabetes, cancer, bone resorption diseases, graft vs. host reaction, Alzheimer's disease, stroke, myocardial infarction, ischemia reperfusion injury, atherosclerosis, brain trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock syndrome, fever, myalgias due to HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses or herpes zoster infection in a mammal comprising administering an effective amount of a compound of Claim 16.

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23. A method for prophylaxis or treatment of pain comprising administering an effective amount of a compound of Claim 1.

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24. A method for prophylaxis or treatment of pain comprising administering an effective amount of a composition of Claim 16.

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